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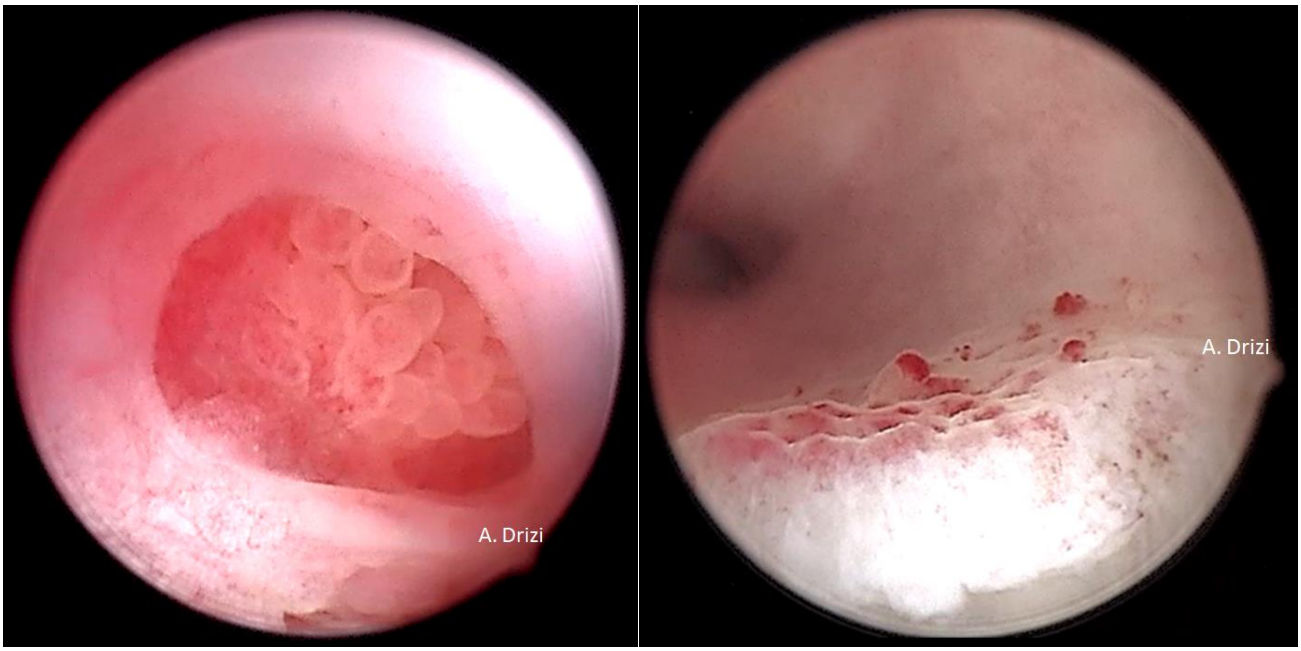

ISSUE 1 Volume 4 (March 2023)

Special Issue

Diagnostic Hysteroscopy

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Go ahead ISGE

As was to be expected, we will also be dealing with the same problems in 2023 as in 2022. ISGE has its core task in imparting knowledge and training, but must take into account the wide range of different global conditions. Traditionally, ISGE tries to get involved in countries that have fewer resources available. In addition to the already successful project "Diplome Universitaire" in Cameroon, in which we have been successfully supporting further training for local doctors for several years, we have now started another project in Zanzibar. Here, too, the principle of "train the trainers" should be given top priority. Medical Director Prof. Bruno van Heerendael and Executive Director Paula Simons, were on site and launched the project with the President of Zanzibar . We are pleased to be able to find many volunteers from our growing community who support the project. In March, the first participants from Zanzibar took part in the Diplome Universitair in Youndé.

All countries are suffering from the current high energy prices and the battle for resources has unfortunately become even tougher. The countries that are already disadvantaged therefore need all the more support. For ISGE, it is an important task to help more people receive surgical assistance. Therefore, we also support vaginal hysterectomy projects. Especially in countries with low incomes and low electrification, traditional techniques are more likely to be implemented than high-tech surgery. Therefore, in our logo you will find "promoting vaginal hysterectomy". It is a great step forward for many regions to be able to offer these techniques and avoid the riskier laparotomy. Interestingly, the industrialized nations are now rediscovering this access route with endoscopic support (vNotes). However, these techniques are less helpful for resource-poor countries, because without special instruments, the technique may be inferior to classical vaginal surgery.

As always at this point, I invite you to become part of the ISGE family. Every little contribution counts. The more we are, the more we can do. **Come to ISGE!**

Before a good surgical treatment, there is a "good" diagnosis. In gynecology, hysteroscopy is an established method and can be carried out with relatively simple means of diagnosis. From placenta residue to chronic infections or adenomyosis, fibroids as well as hormone problems, hysteroscopy can be used to make precise diagnoses. Therefore, we have designed this issue as a special issue and dedicated it entirely to hysteroscopic diagnostics. Our board member, Dr Amal Drizi, was in charge of the design. We would like to thank her and the many authors for this, in my opinion, very successful edition of TheTrocar. I hope you enjoy reading the articles and hopefully new insights.

Yours

Guenter Noé

Editor in Chief

Index: Issue 1 Volume 4 The Trocar — March 2023

The frontpage shows: 1) glandular island ectropion 2) micropolyps + hyperemia + edema

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THE INTERNATIONAL SOCIETY FOR GYNECOLOGIC ENDOSCOPY
PROMOTING VAGINAL SURGERY

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Why a special issue on diagnostic hysteroscopy?

Letter to the editor

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Endoscopy is the branch of medicine where the inside (endo) of an organ's cavity is viewed (scopy) and eventually treated. Depending on the targeted organ, different terms have been defined: colonoscopy; arthroscopy; laryngoscopy to name just a few. Hysteroscopy is the branch of endoscopy dedicated to the uterine cavity. Etymologically, it derives from "scopy", which means "viewing", and "hystero" which means "uterus". It literally means visualization and examination of the uterus and by extension, the surrounding cavities (vagina, cervix and part of the tubes).

Visual examination of a part of the organism is a very important discipline in medicine. As opposed to "endo", the visual examination of the external covering of the human body, the integument, is a whole specialty in medicine termed dermatology. It has tremendously evolved throughout the centuries and possesses large references about visual diagnosis of skin disorders, as well as their treatment. When taking a closer look at this specialty, it is a fact that all dermatologists know by heart the composition of the integument, the fundamental lesions to target and biopsy in order to the diagnosis-making process. Dermatology is an independent specialty that cannot be replaced by maxillofacial surgery for instance. The latter is led by surgeons who do not have the expertise of a dermatologist in terms of skin examination, but do better know the rules of how to properly remove pathology. Although the two specialties have different scopes and skills, they complete one another.

Hysteroscopy however, is like dermatology being led by surgeons. In fact, today's opinion-leaders in hysteroscopy seem to have a typical "surgeon mindset", with a particular interest in advanced uterine surgery, but with limited interest in diagnosis. This makes sense as surgery and diagnosis consist of two different approaches requiring different backgrounds and skills. This

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separation has already been made, not only in dermatology/maxillofacial, but also in nephrology/ urology and in gastroenterology/general surgery. Colonoscopy for instance is the visual examination of the colon-rectum, with identification of the lesions to be biopsied and/or removed. It is performed by gastroenterologists trained in endoscopy, not by surgeons. If cancer is documented however, surgeons take over and remove the colon-rectum under oncological requirements. A surgeon will not be interested in the colonoscopic criteria of medical conditions colonoscopy can diagnose, such as rectocolitis, tuberculosis, Biermer disease etc. Likewise, a gastroenterologist is not supposed to acquire the surgical skills surgeons have. This is why separating the two disciplines has allowed expansion and progress in both.

Unfortunately, this separation has not yet been officially acknowledged in "hysteroscopy/ intrauterine surgery", at the detriment of hysteroscopy as a diagnostic tool. Any gynecologist who would dive in the depths of endometrial physiology, histology and histopathology could clearly confirm that our practice of hysteroscopy is not based on a deep knowledge of these basics. It becomes factual that we are not doing hysteroscopy, but rather under vision intrauterine procedures. Hysteroscopists worldwide are dealing with the endometrium like a dermatologist, who has a poor idea of what the skin is made of, would deal with his specialty. Not to mention that unlike the skin, the endometrium undergoes cyclical changes, which make it even more complex to comprehend. Despite that, there is to date a lack of proper training for hysteroscopists in this area.

Today, hysteroscopy being led by expert uterine surgeons is limiting the development of the diagnostic aspect of medical conditions, such as dysfunctional and inflammatory disorders. To date, the term "diagnostic hysteroscopy" has become almost exclusively linked with the instrumental and technical issues, including indications and pain management (1-7). Although targeted biopsy has received attention and been improved in the last years, still mostly in terms of technique and comfort (8;9). However, in the absence of evident intrauterine anomalies such as overgrowths, adhesions or malformations, there are to date no specific guidelines for the assessment of the mucosa itself to define the optimal sites for targeted biopsy in diagnostic hysteroscopy. In "an empty cavity", hysteroscopy is usually conducted in a "come in – come out" fashion and blind sampling with Pipelle continues to be performed at the end of the procedure. The technical aspect of the procedure has been much more invested than the analytic aspect of its diagnostic possibilities. This is quite problematic and is limiting the potential of the procedure, especially in medical conditions, such as dysfunctional disorders in symptomatic patients suffering from abnormal uterine bleeding (AUB) or unexplained infertility. Analogically, it looks more like a dermatologist who views inflammatory lesions to which a histological etiquette is requested, yet instead of performing a targeted sampling within the observed lesions, the skin would be blindly and randomly scratched anywhere else.

It is a regrettable fact that there is to date no standardized methodology to examine the endometrium in respect to its basics of physiology and histopathology (10). Uterine surgery continues to shade diagnostic hysteroscopy and the latter continues to receive limited attention and to be performed by

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practitioners who have a modest knowledge on the different facets of the endometrium. Additionally, many colleagues are persuaded there is no point in putting efforts into developing diagnostic hysteroscopy because the final diagnosis belongs to histopathology. The lack of education in the areas of endometrial physiology and histopathology has turned hysteroscopists into passive actors, completely relying on the pathologist's conclusions. This is why diagnostic hysteroscopy has not much progressed as opposed to the other branches of endoscopy, such as colonoscopy and fibroscopy.

As a thoughtful practice of diagnostic hysteroscopy by a warned hysteroscopist can considerably transform the diagnostic and decision-making process for the patient's benefit (11), this special issue will exclusively be dedicated to the diagnostic opportunities hysteroscopy provides. It aims at providing an educational content for a more standardized practice of diagnostic hysteroscopy in a way which is founded on the available evidence, including basic sciences. We advocate separation of diagnostic hysteroscopy from uterine surgery, as well as the importance of a proper training of colleagues with a special interest in diagnostic hysteroscopy. Hopefully, this will allow the latter to evolve like all the other branches of diagnostic endoscopy.

Amal Drizi

Guest editor of TheTrocar's special issue on diagnostic hysteroscopy.

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Diagnostic hysteroscopy: patient assessment and preparation.

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The authors declare no conflict of interest.

Abstract

This article provides a brief and evidence-based overview of the basic principles related to the evaluation and preparation of the patients planned to undergo diagnostic hysteroscopy. Anamnestic data should be taken and analyzed, general and pelvic physical examination performed, pregnancy and genital infections excluded, and a gynecological ultrasound realized. The patients should be advised about alternative diagnostic procedures and informed in details about the benefits, expected success of diagnostic hysteroscopy, but also about possible discomfort/pain and complications. In addition to adequate patient counseling, preparation for a successful hysteroscopy includes proper timing of the procedure and cervical ripening in selected women. Analgesia is addressed in a separated review of this journal issue. There are no evidence-based indications for antibiotic prophylaxis to be given before or during hysteroscopy.

Key words:

Diagnostic hysteroscopy; patient assessment; evaluation; patient preparation.

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Introduction:

Hysteroscopy provides an accurate, minimally invasive and direct-vision approach to diagnose structural endometrial and uterine cavity pathologies associated with abnormal uterine bleeding (AUB) and reproductive failure, which may be congenital (*e.g.,* uterine septa) or acquired (*e.g.*, polyps, fibroids, adhesions) (1). Currently, in most cases, diagnostic hysteroscopy is performed on an outpatient basis, as a safe and well-tolerated technique, thanks to the progress of endoscopic technology, the use of minimal caliber instruments as well as the vaginoscopic approach to introduce the hysteroscope into the cervical canal and uterine cavity (2, 3, 4). As with any procedure involving uterine instrumentation, it requires appropriate preprocedural assessment and preparation of the patients to improve not only the diagnostic success but also the technique safety and patient comfort (5). The aim of this article is to provide a clear, brief and evidence-based overview of the basic principles related to the evaluation and preparation of the women undergoing hysteroscopy for diagnostic purposes.

Methods:

A non-systematic review of the literature published in English language until November 1st, 2022 was performed by searching PubMed using 3 search term combinations: (1) diagnostic hysteroscopy AND guidelines; (2) diagnostic hysteroscopy AND patient evaluation OR patient assessment; and (3) diagnostic hysteroscopy AND patient preparation. The abstracts were analyzed, pertinent articles included and the references of all included articles were also searched in order to find additional relevant articles. Through multiple cycles of literature review and discussion between the authors, consensus answers were reached to questions related to the clinical and imaging assessment of women before hysteroscopy, patient counseling, diagnostic hysteroscopy timing, cervical preparation and prophylactic antibiotic prescription. Pain management is addressed in a separated review of this journal issue.

Literature review:

Preprocedural patient evaluation

The patient evaluation prior to performing diagnostic hysteroscopy aims to thoroughly characterize women who are scheduled for this exam, reducing the likelihood of both procedural failure and complications. In this important phase, anamnestic data are taken and analyzed, physical examination performed and pregnancy reasonably excluded (5). On this occasion, it is adequate to check whether gynecological (cervical) cancer has been adequately screened and to carry out screening if not. Before the diagnostic hysteroscopy, an anatomical examination of the uterus is performed, whereby ultrasound represents the first-line imaging approach (6).

Medical history. Medical history taking is the initial step in the patient evaluation. Comprehensive data should be properly structured. Particular attention should be paid to the symptoms [all, but especially those that indicate hysteroscopy (Panel 1.)] and previous treatments, as well as obstetric/gynecological history, comorbidities, previous surgeries, medications, allergies and habits (6).

Physical examination. A general and complete abdominal and pelvic physical examination should be performed. Particular attention should be paid to the characteristics of the uterus that affect the performance of the hysteroscopic technique, including the position, size, mobility and cervical patency (6). It is appropriate to carry out cervical cancer screening on this occasion, if

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indicated and not previously performed in accordance with current national/international guidelines (7). Observation of the signs of cervicitis indicates the need to sample material for cervical cultures. Infectious and other contraindications for hysteroscopy are shown in **Panel 1**.

Indications	Signs and symptoms indicating endometrial/intracavitary pathology • Abnormal uterine bleeding (AUB) • Infertility and repetitive abortions • Cervical and/or intracavitary adhesions • Retained contraceptive intrauterine device / other foreign bodies Other technique indicating endometrial/intracavitary pathology • Ultrasound indicating endometrial/intracavitary pathology • Gynecological cytology: atypical glandular cells (AGC) Follow-up • Conservative management of endometrial hyperplasia / cancer in selected patients
Contraindications	Viable intrauterine pregnancy Active pelvic infection (including genital herpes) Known cervical cancer

Panel 1. Indication and contraindications for diagnostic hysteroscopy

Laboratory testing. For the performance of diagnostic hysteroscopy, especially in outpatient settings, no laboratory tests are required, unless it is indicated by specific anamnestic data or clinical circumstances. In women of reproductive age, if the procedure is not scheduled immediately after menstruation, a pregnancy test may be needed (5).

Anatomical uterine assessment by imaging. Although hysteroscopy is considered the diagnostic gold standard for endometrial and intracavitary pathology, **ultrasonography** represents the first-line assessment tool (along with the clinical examination) for anatomical evaluation of the uterus in patients with symptoms and signs suggestive of endometrial and/or myometrial lesion(s). Well-known ultrasound advantages include its availability, noninvasiveness, reliability and cost-effectiveness (8). Transvaginal ultrasound (TVUS) offers better resolution then abdominal ultrasound (9), which is useful, due to its wide vision, to exclude or, when present, to evaluate pathology extending beyond the pelvis (6). A

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consensus opinion from the International Endometrial Tumor Analysis (IETA) group on the terms, definitions and measurements to describe the sonographic features of the endometrium and intrauterine lesions was published in 2010 (10). The Morphological Uterus Sonographic Assessment (MUSA) paper, published in 2015, provides a consensus statement on terms, definitions and measurements that can be used to describe and report normal and pathological myometrial findings during an ultrasound examination (9). The use of standardized methodology to assess the uterus (both endometrium and myometrium), as well as common definitions and terminology to report findings is highly desirable, resulting in reduced intra- and inter-observer variability and better communication between sonographers, sonologists, gynecologist, other clinicians and researchers (6, 9, 10). The typical ultrasound features of endometrial atrophy, polyps, hyperplasia and cancer, and intracavitary leiomyomas, in symptomatic and asymptomatic women, have been described using the IETA terminology (11, 12). In patients with AUB, the TVUS detection of some easy-to-assess IETA features (endometrial thickness < 3 mm, three-layer pattern, linear midline and single vessel without branching) makes endometrial cancer unlikely (11). When endometrial malignancy is suspected by ultrasound, blind sampling is often performed, followed by diagnostic hysteroscopy and direct-vision biopsy in cases where the diagnosis of malignancy is not confirmed by pathohistological examination. Hysteroscopy is a safe diagnostic method and has no significant effect on the prognosis of early-stage endometrial cancer (13).

Contrast-using saline-infusion sono-hysterography (SIS) and gel-instillation sonohysterography, in two (2D) or three dimensions (3D), are very accurate diagnostic procedures to describe submucous leiomyomas (14, 15, 16), cesarean scar niche (17, 18, 19) and congenital uterine malformations (20, 21). For instance, in accordance with a Cochrane systematic review and a 2017 systematic review and meta-analysis of 1398 citations and 5 studies, high-quality evidence supports that SIS is equally performant as hysteroscopy to diagnose submucous leiomyomas (6, 15, 22). By defining the extent to which a leiomyoma protrudes into the uterine cavity and, in parallel, the depth of myometrial penetration by the lesion, SIS provides the information analog to that from the combined use of hysteroscopy and TVUS (23). If an atypical intracavitary leiomyoma is observed during the pre-hysteroscopy ultrasound assessment, the 2017 ISGE guidelines for the assessment of the sarcoma risk can be used (24).

Informed consent and patient preparation for diagnostic hysteroscopy

Diagnostic hysteroscopy is a minimally invasive and generally safe procedure (5). However, patients planned to undergo diagnostic hysteroscopy should be advised about alternative diagnostic procedures, as well as informed about the benefits and expected success of the procedure, but also about possible discomfort/pain and complications. They should be informed about the possibility of abandoning or prematurely ending the procedure due to complications, intolerance or the impossibility to introduce safely the hysteroscope into the uterine cavity. The patients should agree to undergo eventual laparoscopy or laparotomy if necessary to rule out iatrogenic visceral or vascular pelvic injury. The patient should receive an explanation about the limits for hysteroscopy, after which the procedure must be stopped immediately even if it is not completed due to the complications that could arise or to the patient's significant

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discomfort (detailed in the articles "complications" and "pain management of this monothematic issue). It should be noted that in such a case it will be necessary to schedule another hysteroscopic procedure. Also, the patient should receive information about transient symptoms (primarily pelvic discomfort and spotting) that she may have even after an uncomplicated hysteroscopy, about the expected duration and ways of controlling the discomfort, as well as about the expected time for returning to daily routines and work. The most common reasons for failure to complete outpatient hysteroscopy are pain, cervical stenosis and poor visualization (25). Thus, the preparation for successful ambulatory hysteroscopy includes adequate patient counseling, procedure timing, considerations related to pain management, and cervical preparation in selected women.

Timing and endometrial preparation. While in postmenopausal patients, diagnostic hysteroscopy may be performed at any time, in premenopausal women, specifically the follicular or luteal phase may be of interest to study (26). Most authors perform hysteroscopic examinations in the proliferative phase, when the mucosa is thinner, in order to avoid misinterpretation of physiological changes and their confusion with polypoid or hyperplastic endometrium (5, 26). Furthermore, the increased tonus of the cervix caused by the luteal phase progesterone is avoided, thus facilitating the technique (26).

Some women with unpredictable menstruation may be scheduled for hysteroscopy at any time, but visualization may be impaired by active bleeding. Pharmacologic thinning of the endometrium, i.e. pretreatment with combined oral contraceptives, progestins alone or gonadotropin-releasing hormone (GnRH) agonists may improve visualization by thinning of the endometrium (27, 28, 29, 30, 31). Thinning agents should be avoided whenever possible when only diagnostic hysteroscopy is planned, as these hormones may affect endometrial histology.

Cervical preparation. Almost 50% of hysteroscopic complications are associated with difficult insertion of the hysteroscope through the cervical canal into the uterine cavity (25). Many patients do not require cervical dilatation for diagnostic hysteroscopy, particularly premenopausal women undergoing the procedure with a narrow caliber (<5 mm) hysteroscope. Although there is insufficient evidence to support routine cervical ripening prior to diagnostic hysteroscopy, it may be considered for patients with cervical stenosis and/or at increased risk of pain with the procedure (5). According to a systematic review and meta-analysis of 19 studies focusing on cervical ripening before operative hysteroscopy, both pre- and postmenopausal women treated with misoprostol were significantly less likely to require additional mechanical dilation than women who were untreated or treated with dinoprostone or placebo (32). Many practitioners extrapolate these data and apply them to diagnostic hysteroscopy.

The use of misoprostol reduces the hysteroscopy complication rates, being associated with adverse effects, primarily abdominal pain, fever and vaginal bleeding (32). Most often 200 – 400 micrograms of misoprostol are given orally or vaginally, resulting in easier entry into the cervical canal, reduced pain perception, and shorter procedure time (33, 34). Intravaginal misoprostol (400 micrograms) has been shown to reduce pain associated with office hysteroscopy, during and after the procedure, when administered at least 4 hours before the

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procedure (35). Vaginal estrogen (25 micrograms) administered two weeks before the procedure, together with 400–1000 micrograms of vaginal misoprostol applied 12 hours before the procedure, facilitates dilatation of the cervix and significantly reduces pain in postmenopausal women (36, 37).

Prophylactic antibiotics. Infection occurs in < 1% of women undergoing hysteroscopy (38). There is no evidence-based indication for antibiotic prophylaxis to be routinely given before or during hysteroscopy to prevent surgical site infection or endocarditis (5).

Conclusions:

An adequate patient assessment and preparation prior to performing diagnostic hysteroscopy is essential to reduce the likelihood of procedural failure and complications, and to improve patient tolerance and satisfaction. After clinical history taking, physical examination and gynecological ultrasound, confirmation of indications and exclusion of contraindications for diagnostic hysteroscopy, preparation for a successful hysteroscopic examination includes appropriate patient counseling, timing of the procedure and cervical preparation in selected women. This preprocedural phase requires attention, training and updating according to new evidence that may appear in the literature.

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Diagnostic Hysteroscopy: equipment and technique

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Abstract

To date the evaluation of the uterine cavity and of possible intra-uterine pathology is done through vaginal ultrasound, SIS/GIS (Saline infusion Sonography/Gel Infusion Sonography) imaging and through hysteroscopy. The main advantages of diagnostic hysteroscopy (with new generation small-diameter hysteroscopes) are a direct visualisation of the cervical canal and the uterine cavity and the possibility to perform targeted biopsies and even small surgical procedures in an office setting without using any type of anaesthesia or dilatation of the cervical canal.

This article focuses on the equipment and the technique of diagnostic hysteroscopy and how to take an endometrial biopsy.

Key words:

Hysteroscopy; diagnostic hysteroscopy; vaginoscopy; endometrial biopsy; targeted biopsy; grasp technique

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Introduction

To date the evaluation of the uterine cavity and of possible intra-uterine pathology is done through vaginal ultrasound, SIS/GIS (Saline infusion Sonography/Gel Infusion Sonography) imaging and through hysteroscopy (1). To be able to actually 'see' inside the uterine cavity, and even perform targeted biopsies or small surgical procedures, we need specific equipment including a hysteroscope, a cold light source and fibreoptic light cable, a viewing system (with a camera control unit, a video camera and a monitor) for adequate vision and a system for uterine distension (2-6). Specific designed instruments will allow simple procedures – mainly biopsies – which will be addressed subsequently.

Equipment in diagnostic hysteroscopy

We will focus both on the delivery of distension media and on the most commonly used hysteroscopes.

Delivery of distension medium

In modern diagnostic hysteroscopy uterine distension is done using isotonic saline solution. Simple delivery using a syringe (of 50ml) or delivery using gravity with 3L bags 90 – 120cm above the uterus works perfect for simple diagnostic procedures. For small operative procedures in an office setting the slightly higher intra-uterine pressure can be obtained using a manually operated pressure-bag or using an electronic irrigation device/pump (4-6).

When using an electronic irrigation device it is possible to keep a constant pre-defined intra-uterine pressure and it is possible to readjust the different parameters related to the delivery of the distension medium (pressure, flow, suction) during the procedure if needed. When using an electronic irrigation device in a simple diagnostic hysteroscopy we set the pressure as low as 40 – 70mmHg. An intra-uterine pressure <70mmHg prevents passage of the distention medium into the peritoneal cavity and thus lowers the risk of vagal reaction or/and pain (9,10).

Hysteroscopes

Modern office hysteroscopy uses miniaturized hysteroscopes with a 2.0mm – 4.0mm diameter. Hysteroscopes are available in rigid, semirigid and flexible design and are available with a single-flow sheath or with a continuous-flow two-sheath design with working channel (4-6).

The high quality image transmission system in rigid hysteroscopes is based on the Hopkins optical system ie glass lenses alternating between air spaces. On the other hand the semirigid and flexible hysteroscopes are composed of thousands of optical fibres and a single lens at the distal tip. Rigid hysteroscopes are available with viewing angles of 0°, 12° or 30°.

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Semirigid and flexible hysteroscopes do always have a 0° viewing angle (4-6).

The hysteroscopes which are commonly used for office diagnostic (and operative) procedures – and that have inspired the world's endoscope manufacturers - are the following:

1. BETTOCCHI Operating Hysteroscope with Continuous flow – Size 5 and Size 4 (Karl Storz SE & Co.KG, Tuttlingen, Germany) **(Fig. 1a - b)**
   The 'Bettocchi Size 5' has a 2.9mm scope with 30° foroblique viewing angle and an outer diameter of 5mm. The 'Bettocchi Size 4' has a 2.0mm scope with a 30° foroblique viewing angle and an outer diameter of 4mm. Both hysteroscopes are available with two sheaths - one for inflow and the other for the outflow and with a 5Fr working channel. Both hysteroscopes have an oval shaped profile that can be of help in introducing and advancing the hysteroscope through the cervical canal (2,4,5).

2. TROPHYscope - Campo Compact Hysteroscope (Karl Storz SE & Co.KG, Tuttlingen, Germany) **(Fig. 2)**
   The Trophyscope has a 2.0mm scope with an integrated inflow channel (without any sheath) - the outer diameter is 2.9mm and thus very useful for pure diagnostic hysteroscopy. If necessary there are two types of outer sheaths that can be loaded onto the 2.9mm single-flow scope – a continuous-flow 3.7mm diameter sheath or a continuous-flow 4.4mm operating sheath with 5Fr working channel. These outer sheaths can be loaded onto the 2.9mm single-flow scope in an non-active position and can, if required, with a simple push on the button be switched to its active position (2,4).

3. GYNECARE VERSASCOPE Hysteroscopy System (Ethicon Inc., Johnson & Johnson, NJ, USA) **(Fig. 3)**
   The Versascope system has 2 components: a 1.8mm diameter reusable semi-flexible stainless steel tube containing 50.000 fibre optics and a disposable single use sheath. The sheath has a expandable operating/outflow channel up to 7Fr allowing the use of 5 - 7Fr instruments for biopsies or operative procedures. The total outer diameter of the Versacope system is 3,5mm (2).

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Fig. 1a Bettocchi continuous-flow Operating Hysteroscope – Size 5 (Karl Storz SE & Co.KG, Tuttlingen, Germany)

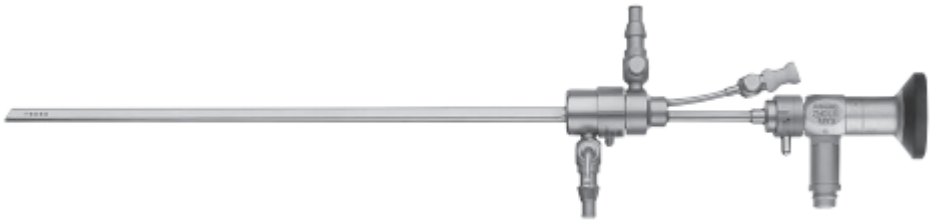

Fig. 1b Bettocchi continuous-flow Operating Hysteroscope – oval shape (Karl Storz SE & Co.KG, Tuttlingen, Germany)

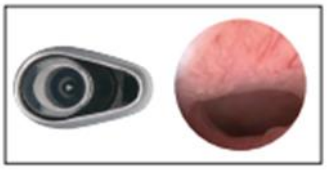

Fig. 2 Campo Trophyscope (Karl Storz SE & Co.KG, Tuttlingen, Germany)

Fig. 3 Gynecare Versa scope Hysteroscopy System (Ethicon Inc., Johnson & Johnson, NJ, USA)

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Miniaturized mechanical operating instruments

Miniaturization of mechanical instruments to the 5Fr dimension has made it possible to perform operative procedures during office hysteroscopy. They are introduced into the working channel of the operating hysteroscope and make it possible to perform biopsies, polypectomies, the retrieval of 'lost' IUD's, the lysis of small adhesions and septa. The mechanical 5Fr instruments most commonly used are: the toothed grasping forceps (also called the alligator forceps), the pointed and the blunt scissors and the tenaculum grasping forceps (Hesseling forceps) **(Fig. 4)** (2,4,5).

Fig. 4 5Fr mechanical operating instruments (Karl Storz SE & Co.KG, Tuttlingen, Germany)

Miniaturized bipolar electrodes

In 1997 a dedicated high-frequency bipolar generator called Versapoint (Gynecare, Ethicon) was launched to be connected not only to a bipolar loop for resection but also to the newly designed bipolar Versapoint electrodes known as

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the Twizzle, the Spring and the Ball electrode **(Fig. 5)**. These disposable 5Fr bipolar electrodes can be introduced into the working channel of the operating hysteroscope and so do expand the range of surgeries that can be performed in an office setting. The Karl Storz Company (Germany) followed in 2005 with the development of miniaturized re-usable 5Fr bipolar electrodes **(Fig. 6)** (2,4,5).

Fig. 5 disposable bipolar 5Fr Versa point electrodes (Gynecare Ethicon Inc., Johnson & Johnson, NJ, USA)

Twizzle Spring Ball

Fig. 6 re-usable bipolar 5Fr electrodes (Karl Storz SE & Co.KG, Tuttlingen, Germany)

5Fr bipolar dissection electrode 5Fr Gordts/Campo bipolar ball electrode

Diagnostic hysteroscopy – the technique

No-touch or 'vaginoscopic' approach

The vaginoscopic technique, introduced by Stefano Bettocchi, makes it possible to approach the cervix and then the uterine cavity without a speculum and without a tenaculum. This reduces the anxiety of the patient and allows for maximal relaxation. The absence of the speculum allows greater maneuverability of the scope. This is an advantage when the uterus lies in an extreme anteversion or retroversion. Vaginoscopy is possible with a 0° scope but is easier with a 30° foroblique scope. The learning curve is rapid (3,6).

Without performing any disinfection, the hysteroscope is positioned at the introitus. The vagina is distended with saline solution and with the same pressure used for the uterine cavity (40 – 70mmHg). The hysteroscope is then advanced posteriorly in the fornix posterior and then slowly backwards to locate the external os. Once this is correctly visible the tip of the scope is

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introduced into the cervix and, following the anatomy, gradually advanced further to reach the internal os and the cavity (3,6).

Intracervical advancement of the hysteroscope is potentially the most difficult part of the procedure. The key point is to avoid trauma to the fragile endocervical mucosa as this stimulates pain, can cause bleeding and poor view and can possibly predispose to false passage formation. Proceed slowly allowing the distension medium to open the cervix. When using a oval profile scope a 90° rotation of the instrument can adapt the scope to the major transverse axis of the internal os that appears oval. If synechiae or stenosis of the cervical canal are present use the alligator forceps or the scissors to free the passage instead of using force to overcome them (6).

After passing the internal os a few seconds wait will be sufficient to obtain the distension of the uterine cavity. Proceed from the internal os upward following the axis of the uterine body and avoid touching the uterine wall. It is essential to let the distension medium wash the uterine cavity so to identify the uterine landmarks – fundus, cornua and tubal ostia, anterior, posterior and lateral walls. The 30° optic allows easy visualization of all the uterine walls by rotating the optic gently on its axis to the right and to the left. On the contrary, the same vision with a 0° optic is possible only by moving the entire instrument to the right or to the left with lateral movements resulting in more discomfort for the patient (6).

After a general structural assessment attention should be drawn to focal lesions (polyps, fibroids, adhesions, adenomyosis), to congenital anomalies and to the endometrium. Hysteroscopic evaluation of the endometrium can be done with the hysteroscope at a small distance (1-2mm) to evaluate the surface, color, glandular openings and superficial vessel pattern.

Once inspection of the uterine cavity has been completed, the hysteroscope is slowly withdrawn into the cervical canal which can be inspected again (6).

How to take an endometrial biopsy?

One of the main advantages of office hysteroscopy is the possibility to perform targeted biopsies under direct visualization.

The three most common techniques to perform a targeted biopsy sampling are the following (2,7,8):

1. the Punch biopsy: uses a spoon biopsy forceps to biopsy the endometrium. The main disadvantage is the small, often not representative biopsy sample.

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2. the Grasp biopsy **(Fig. 7)**: uses the toothed grasping forceps (alligator forceps). The grasp biopsy technique is preferred over the punch biopsy technique as it permits removal of larger portions of tissue. This is possible because of the length of the toothed jaws that are double in length in comparison with the jaws of the spoon biopsy forceps and the application of a specific grasp technique. The alligator forceps is positioned with the jaws open at the level of the endometrium. With open jaws the forceps is advanced (plowed) across the tissue for about 1-2 cm. At this point the jaws are closed again and the biopsy is grasped. The retrieval of the biopsy from the uterine cavity is done - together with the entire hysteroscope - without retracting the tip of the forceps into the operating channel of the hysteroscope.
3. the Cutting biopsy: uses a hysteroscopic scissors or a bipolar 5Fr electrode to cut/individualise an endometrial area. The retrieval of this (larger) biopsy has to be done through the alligator forceps or by the tenaculum grasping forceps.

In 2019 Vitale did propose another grasper for taking endometrial biopsies: the Biopsy Snake Grasper (12). It is a robust, easy-to-use grasper with a central serrated tip and 2 sharp-edged jaws that completely encompass the tip when they are clenched. It can be used through all 5 Fr working channels

Recent advances in miniaturization of hysteroscopic equipment have yet resulted in the availability of mini-resectoscopes **(Fig. 9)** and of small-diameter 'tissue removal systems' **(Fig. 10)**.

Fig. 7: 'grasp biopsy technique'

a the forceps is positioned with jaws open

b the forceps is advanced with open jaws for about 1 – 2cm

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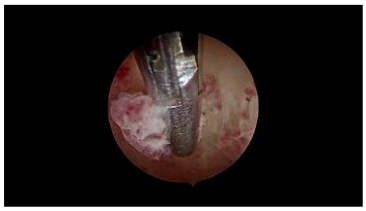
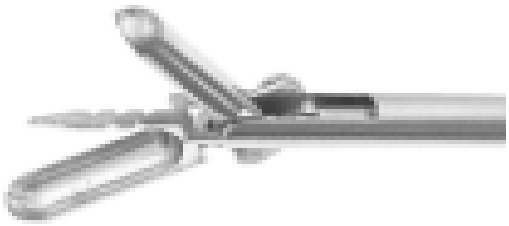
c the jaws are closed again and the biopsy is grasped



d Retrieval is done together with the entire hysteroscope

Fig. 8: 'the Biopsy Snake Grasper'



Probably in the near future these new hysteroscopic small-diameter tools will enable us to perform diagnostic hysteroscopy followed by extensive biopsy sampling and a one-step treatment of larger intra-uterine pathology outside of the operation room without anesthesia and with little or no dilatation (2,11).

Fig. 9 mini-resectoscopes
Gubbini Ellipse System 14,9Fr (Tontarra Gmbh – Germany).

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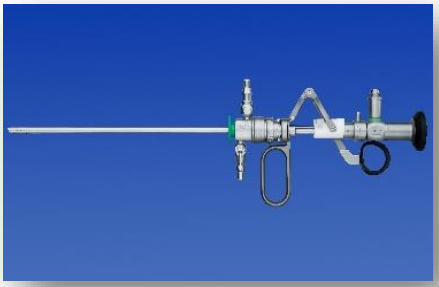
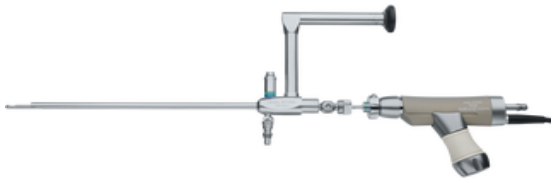


15Fr min resectoscope (Karl Storz SE & Co.KG, Tuttlingen, Germany)

Fig. 10 small-diameter 'tissue removal systems' Truclear ® Elite mini hysteroscope (5,7mm) (Medtronic)



19 Fr Intrauterine Bigatti Shaver (Karl Storz SE & Co.KG, Tuttlingen, Germany)

Conclusion

Numerous technical innovations, in particular the development of small-diameter hysteroscopes equipped with a working channel, allow not only evaluation of the cervical canal and the uterine cavity but also to perform biopsies and to treat intra-uterine pathology without anesthesia in an outpatient setting.

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Diagnostic hysteroscopy: pain management

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Abstract

During last years, many innovations have been adopted in order to minimize the pain experienced during office hysteroscopy and to increase its completion rate, such as technical improvements, better tools and several pharmacological and non-pharmacological methods. Up to date, there is still no universal consensus about the most effective way to minimize discomfort during hysteroscopy. This chapter summarized the current recommendation and the most recent clinical data about the reduction of pain and discomfort during and before office operative hysteroscopy, highlighting the pharmacological and non -pharmacological measures.

Key words:

Hysteroscopy; Pain; Anesthetic drugs; Prostaglandins; Antispasmodic and pain medications; non-pharmacological measures.

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Introduction

Hysteroscopy is a common and valuable intervention to diagnose and treat gynaecological conditions arising in the uterus such as infertility, abnormal uterine bleeding and suspected endo cavitary pathologies [1]. Biopsy of the endometrium in case of endometrial anomalies represents another diagnostic purpose of this technique. The outpatient setting in hysteroscopy is also proved to give several advantages, such as: avoidance of general anesthesia, shorter recovery time with immediate return to work or daily activities, higher patient satisfaction and it is more cost-effective. Although in most of women the outpatient hysteroscopy is well tolerated, the pain is still reported as the main limiting factor to the widespread use of this procedure by several papers about the acceptability of this procedure. The most important risk factors associated to pain and discomfort are nulliparity, menopause, presence of cervical synechiae and long operative time. On the contrary, patients who had at least one previous vaginal delivery seem to have a best tolerance to the procedure. During last years, many innovations have been adopted in order to minimize the pain experienced during this procedure and to increase its completion rate, such as technical improvements, better tools and several pharmacological and non-pharmacological methods. Up to date, there is still no universal consensus about the most effective way to minimize discomfort during hysteroscopy.

This chapter summarized the current recommendation and the most recent clinical data about the reduction of pain and discomfort during and before office operative hysteroscopy, highlighting the pharmacological and non - pharmacological measures.

Pathophysiology of pain during hysteroscopy

The nociceptive signal concerning intraperitoneal structures is conducted to T12-L2 spinal ganglia by visceral afferent fibers through both inferior and superior hypogastric plexus. The passage of the hysteroscope into the cervical canal, the uterine cavity distension, and peritoneal irritation due to spill of fluid into the abdomen are reported as the main responsible for pain originating during hysteroscopy. On the contrary, the increase in prostaglandins production due to endometrial damage is advocated by some authors as the cause for the delayed pain after 30 min from the procedure [2].

Vaginoscopy technique

Diagnostic hysteroscopy should be performed following the “no touch” approach to reduce the discomfort of the patient. This approach consists of inserting of hysteroscope into the vagina under visual control without touching the labia

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and vaginal walls [3]. It is well established that the introduction of hysteroscope by vaginoscopy provides less pain when compared to the use of speculum and tenaculum [4]. The use of smaller instruments (3.5 mm vs 5 mm) is also associated to reduction in painful experience as reported by several series with a lower pain score at the visual analogue scale (VAS), especially in nulliparous and menopause subgroups [5,6]. The use of a distension medium during the procedure is necessary since the uterine cavity is a virtual space which requires to be distended. To date, the saline solution media is considered superior to CO_2 according to the intensity of pain perception, incidence of shoulder pain and patient's satisfaction as described in the metanalysis of Craciunas et al. [7]. This is probably related to the easier insertion of instruments through cervical canal when saline solution is used [5]. The use of CO_2 was also associated to most frequent side effects such as vasovagal reaction, bleeding and shoulder pain.

These results appear in contrast with most recent data published by Mazzon et al. and Tagliaferri et al. in which the women that underwent hysteroscopy with CO_2 experienced a significant lower pain [6,8]. The reasons of these findings was explained by the significant shorter time of hysteroscopy performed with carbon dioxide. Several studies were also conducted on the relation between pain and pressure or temperature of fluid distension media used during diagnostic hysteroscopy [9,10]. Higher pressure (> 70 mmHg) seems to be responsible for an increase in pain experience during the procedure due to sudden distension of uterine walls. On the other hand, the pressure levels is not related to an increase of pain perception 30 minutes after the procedure [9]. For this reason, the operator should start the diagnostic hysteroscopy with lower pressure and gradually increase it until an adequate vision is reached. Regarding the temperature, the use of warmed saline solution was not effective in reducing discomfort compared to saline at room temperature [10].

Regardless the diameter of instruments or characteristics of distension media used, performing a correct technique to reach the uterine cavity is considered the most important factor in pain experienced by patients. Particularly, the passage of hysteroscope through the cervical canal is reported as the most painful step of the procedure. In order to reduce the pain it is of the utmost importance the correct placement of the hysteroscope in the cervical canal which should avoid to touch the cervical wall.

Pharmacological treatment

Anesthetic drugs

Various methods of analgesia have been reported in literature to suppress the pain

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associated with hysteroscopy. In a recent meta-analysis including 2610 patients De Silva et al. showed that all routes of administration including topical application (to the ectocervix and / or transcervical instillation) and injection (intracervical, paracervical and intracornual blocks) of lidocaine, mepivacaine, prilocaine and bupivacaine achieved a statistically significant reduction in pain during office hysteroscopy. However, mepivacaine and bupivacaine were the only specific local anesthetics that produced a statistically significant reduction in post-procedural pain scores [11]. Similarly, in the meta-analysis by Cooper and coll. was reported that paracervical and intracervical injection of local anesthetic drugs reduced pain during outpatient hysteroscopy and the meta-regression analysis showed that paracervical injection was significantly more effective than the other methods. In contrast, the intracavity instillation of local anesthetic and anesthetic applied topically to the cervix did not substantially reduce the pain during the procedure [12]. In line with these results in randomized, double-blind, placebo-controlled trial the application of lignocaine gel 2% to the cervix during outpatient hysteroscopy was not effective in reducing overall pain and pain in any individual step of the procedure compared to the placebo [13]. According to literature data, the instillation of intrauterine lidocaine injected directly to the cervix or given as a paracervical block few minutes before the procedure would seem to be associated with the reduction of pain during the procedure, however the act of intrauterine instillation of lidocaine can be painful. For this reason many authors have researched an alternative anesthetic methods. In a recent study 10 mL of lidocaine 2% added to 1000 mL of saline solution was used as the distension medium. The study group had an average rise of 1.9 in the VAS score after the procedure compared with 2.9 in the control group ($p = 0.033$). There was also a nonsignificant trend for shorter duration of hysteroscopy in the intervention group compared with the control group (180.1 vs 222.1 seconds, $p = 0.08$) and no side effects were recorded in either group [14]. In contrast, the use of sublingual buprenorphine for pain relief in office hysteroscopy has not shown encouraging results.

The tablet of buprenorphine 0.2 mg had no benefit in reducing the pain associated with hysteroscopy and was associated with adverse effects (e.i. drowsiness, nausea or vomiting) and a lower level of satisfaction [15].

Prostaglandins for cervical preparation

Currently there is insufficient evidence to recommend routine mechanical cervical dilatation prior to outpatient hysteroscopy, especially in the context of modern miniature hysteroscopes which avoid this unnecessary step. Regarding the relationship between the use of cervical preparation with prostaglandins and

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the reduction of pain during hysteroscopy discordant results are reported in literature. In a randomized, double-blind, placebo-controlled clinical trial by Nakano et al. including 158 postmenopausal women, 79 of these received 200 mg of vaginal misoprostol before diagnostic hysteroscopy. The procedure was performed by a rigid hysteroscope, based on a 2.9-mm rod-lens system with a 30° foroblique view, a Pozzi tenaculum forceps was used to grasp the uterine cervix and carbon dioxide was used as the distension media with a 50 to 60-mm Hg flow that did not exceed 100 mm Hg. The authors reported that the use of misoprostol did not reduce pain intensity neither the duration of the procedure and was associated with adverse effects, such as genital bleeding, abdominal cramping pain, and diarrhea [16]. On the contrary, in a similar study the authors included 100 postmenopausal patients (n. 50 = control group; n. 50 = study group) and the use of vaginal dinoprostone 3 mg administered 12 hours before diagnostic hysteroscopy was significantly correlated to the reduction of the intensity of pain. The procedure was conducted by a vaginoscopic approach without speculum and tenaculum, using a rigid 30˚ angled, 2.9-mm hysteroscope with a 4-mm outer sheath, normal saline was used to distend the uterine cavity, and the intrauterine pressure was maintained at 50 mmHg with an electronically controlled pump to prevent excessive distension of the uterine wall [17]. Similar results were reported in the study by Inal et al., which demonstrated the superiority of 10 mg vaginal dinoproston over 400 µg vaginal misoprostol administered 6 to 8 hours before diagnostic hysteroscopy in nulliparous women inducing more cervical priming and increasing cervical width before the procedure [18].

Antispasmodic and pain medications

Antispasmodics are commonly used in outpatient gynecologic procedures due to their specific action on the cervical–uterine plexus, reducing spasms achieved by cervical smooth muscle cells and at the same time acting as a bland cervical dilator. In a randomized controlled trial by Sharma et al. the antispasmodic drotaverine, administered orally with mefenamic acid before in-office hysteroscopy and endometrial biopsy, was compared to paracervical block achieved with 1% lignocaine. The oral drotaverine plus mefenamic acid was more effective than paracervical block in reducing pain perception [19]. Moreover, in a recent randomized double-blind placebo-controlled trial the oral antispasmodic hyoscine butyl-bromide (HBB) was not effective as the oral diclofenac potassium in the reduction of pain perceived by the patients undergoing office hysteroscopy [20]. Intramuscular injection of phloroglucinol improved the cervical width throughout a wider dilatation, helping to gain an easier cervical passage and reducing pain and discomfort. This route of administration represents an alternative to oral or vaginal

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misoprostol, with lower side and adverse effects [21]. The use of pre-medication with non-steroidal anti-inflammatory drugs (NSAIDs) or paracetamol was also investigated over the past years. The use of mefenamic acid administered before outpatient hysteroscopy was investigated and any significant lowering in patient discomfort during or after the examination was reported [22]. A 2017 Cochrane analysis evaluated that there are insufficient data to prove their effectiveness in obtaining pain reduction during the examination [23]. On the other hand, a trial by Abbas et al. showed that the use of oral diclofenac potassium, scheduled one hour before in office hysteroscopy, significantly reduces the discomfort, shortening the procedure time and increasing the level of toleration, when compared to the antispasmodic hyoscine butyl-bromide [24]. In a prospective randomized study the administration of 1 g paracetamol and 600 mg ibuprofen one hour prior to office hysteroscopy was not statistically related to decrease of pain experienced during the test, as well as 5 and 30 minutes after its completion, as assessed by the visual analog scale. However the occurrence of side effects such as nausea, emesis, and hypotension decreased statistically in patients who received analgesia [25]. In addition, the administration of rectal indomethacin has been found effective in reducing pain perceived during office operative hysteroscopy [26]. In a randomized double-blind placebo-controlled trial the use of Celecoxib, a selective cyclooxygenase-2 inhibitor administered orally, was investigated. The use of Celecoxib 200 mg was related to reduction of pain compared to placebo and it was found not inferior to oral Tramadol 100 mg in reducing discomfort or pain during office hysteroscopic surgery [27].

Non-pharmacological measures

Intra-operative music

Regarding non-pharmacological management, several studies evaluated the effectiveness of music in reducing anxiety and pain perception during office hysteroscopy. The randomized controlled trial by Mak et al. showed no positive effect of music regarding pain (p=0.382), anxiety (p=0.491) or satisfaction (p=0.165) [28]. A recent prospective randomized controlled trial conducted on 107 patients (music group n. = 54; control group n. = 53) showed that patients in the music group experienced significantly less pain during outpatient hysteroscopy (VAS score 4.54 ± 2.89 vs 5.88 ± 2.90; P = 0.02). The vital parameters measured before and during hysteroscopy, secondary outcome of the study, were not statistically significantly different between the two groups [29]. The prospective randomized trial by Angioli et al. that enrolled patients undergoing office hysteroscopy using the vaginoscopic approach without any type of anesthesia, reported that women in the music group experienced significantly lower anxiety

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and less pain during the procedure, and a significant decrease in both anxiety and pain scores after hysteroscopy ($p<0.001$) [30]. In summary, there is some evidence that music is effective in controlling pain and anxiety during hysteroscopies.

Transcutaneous electrical nerve stimulation

Transcutaneous electrical nerve stimulation (TENS) consists of the application of a pulsed electrical current through the skin using surface electrodes, a non-invasive form of analgesic treatment. In literature four studies have specifically studied the analgesic effect of TENS during hysteroscopy. De Angelis et al., in 2003, concluded that women assigned to the TENS group experienced significantly less pain than those in the control group [31]. Yilmazer et al., in 2012, studied the effect of TENS in women who underwent a hysteroscopy with biopsy in conjunction with an oral pharmacological treatment. Women reported a significant reduction in the pain they experienced compared to the placebo group 15 min after the procedure [32]. Lison et al., in 2017, showed a significant decrease in the mean pain score among patients in the active TENS group CLIMACTERIC 5 compared to the control group, at every stage of the hysteroscopy procedure [33]. Wang et al., in a randomized controlled trial published in 2022, showed that wearable transcutaneous electrical acupoint stimulation bracelet is related to prevention of postoperative nausea and vomiting in patients undergoing hysteroscopy [34]. According to these studies, this technique, if appropriate TENS parameters are selected so that the proper electrical stimulation dose is applied, can be useful for reducing pain during hysteroscopies because it is clinically effective, non-invasive, and without contraindications.

Hypnosis

Some authors have reported a correlation between the hypnosis and the reduction of pain during hysteroscopy. In a meta-analysis of Schnur et al. hypnosis use reduced discomfort, moreover it had a significant effect on anxiety and pain, some critical limits for the satisfactory completion of hysteroscopy [35]. In a retrospective study conducted by Gauchotte et al. no significant differences were found between the group undergoing to hypnosis and the control group in terms of pain, either during or after the procedure [36]. However, in this study the procedures are limited to hysteroscopic tubal sterilization. In addition, because this was a retrospective study, its conclusions are limited. Randomized controlled studies are needed to better investigate this method.

Viewing the screen during a hysteroscopy procedure

Two studies assessed the impact of the vision of the screen during the hysteroscopy on patient's experience. In the randomized trial by Ogden and

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coll. 157 women undergoing office hysteroscopy were randomly allocated to vision of the screen (n = 81) or not (n = 76). The authors concluded that no significant positive effects are related to the vision of the screen and this may interfere with the patient–physician interaction [37]. On the other hand, Morgan et al. reported that in a group of 30 women undergoing hysteroscopy 10 of these wanted to watch the monitor during the procedure and they said that this solution took their mind off the pain [38].

The vocal–local approach

The vocal–local approach is based on the concept that empathetic attention to the patient is able to reduce pain and discomfort related to the procedure. During the hysteroscopy the operator and the supporting staff should provide emotional support to the woman to reduce the level of anxiety and may also involve the patient directly in the procedure. Evidence shows that a comfortable approach that involves the women directly in what is happening during the gynecological procedure might be able to act increasing patient satisfaction and reducing the need for pharmacological treatments [39]. In accordance with the good practice of pain relief and informed decision making for outpatient hysteroscopy by Royal College one member of the team should be exclusively dedicated to looking after the woman's immediate needs and overall wellbeing rather than concentrating on the technical elements of the procedure [1].

Conclusion

Outpatient hysteroscopy represents a common diagnostic and therapeutic intervention in contemporary gynecological practice. This procedure is well tolerated by the majority of patients, however some women reported distressing experience, due to pain during and before the hysteroscopy. It is generally accepted that the use of the smallest diameter hysteroscopes, the vaginoscopic "no-touch" approach and the low inflow and distention pressures has reduced the discomfort and pain experienced during the procedure. However these measures may not be enough, particularly in nulliparous and postmenopausal patients. The use of local anesthetics through paracervical infiltration appears to be effective, as well as lidocaine added to saline solution used as distension medium. Regarding the usefulness of cervical preparation with prostaglandins prior to the hysteroscopy, the dinoproston appears to be significantly correlated with reduction of the intensity of pain. Also the use of pre-medication with non-steroidal anti-inflammatory drugs (NSAIDs) or paracetamol or antispasmodics drugs is related to the reduction of discomfort and other side effects such as nausea, emesis and hypotension. Particularly, the administration of rectal indomethacin or oral celecoxib has been found effective in reducing pain perceived during office hysteroscopy.

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Moreover, the use of non-pharmacological measures, including music, transcutaneous electrical nerve stimulation and the communication with the patient prior and during the procedure are useful in reducing the anxiety level and discomfort or pain experienced by patients undergoing outpatient hysteroscopy.

However, it is mandatory to screen and identify patients who are at higher risk of high levels of pain experience during office hysteroscopy (i.e. nulliparous or postmenopausal women or patients with a stenotic cervix), in order to choose the most suitable aid to make the procedure more tolerated.

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Diagnostic hysteroscopy: vagina and cervix. Micro-colpo-hysteroscopy

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Abstract

The Authors recall how the vagino-scopic approach to hysteroscopy can highlight macroscopically evident alterations of the vagina and the uterine cervix. The use of the Hamou micro-colpo-hysteroscope allows cellular observation "in vivo", thus allowing an immediate diagnosis of the gravity, the location and the extent of any lesion. The personal experience of the last 42 years with the use of micro-colpo-hysteroscopy and the advantages related to the technique is reported.

Key words: Cervical cancer, Diagnostic Techniques, Obstetrical and Gynecological, Endocervicoscopy, HPV, Human papillomavirus, Hysteroscopy, Microcolpohysteroscopy, Vagina, Vaginoscopy

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Introduction:

Diagnostic hysteroscopy gained considerable momentum when - in 1980 - Jacques Hamou conceived and developed his first Microcolpohysteroscope made by Karl Storz SE & Co KG Tuttlingen Germany.
Until then it was a method reserved for very few gynecologists, which required general anesthesia and the use of the operating room. The reduction of the caliber of the instrument, the improvement of vision thanks to the Hopkins lenses, the distention with gaseous medium (CO2) and the enthusiasm of some pioneers, mainly in Italy, contributed to the spread of the diagnostic method.

Starting in the late 1980s, some of us thought of using the so-called "vaginoscopic approach" to the cervical canal and uterine cavity. In particular, to carry out the exploration of the uterine cavity in women with intact hymen it was decided to use a liquid distention medium to observe the vagina without the use of the vaginal speculum, and - subsequently - proceed through the external uterine orifice in the journey discovering the uterine cavity.

In the following years there were numerous improvements characterized by the further decrease in the diameter of diagnostic hysteroscopes and by surgical techniques that allowed the removal of endo cavitary neoformations, as well as the treatment of some congenital malformations.

Office hysteroscopy allows magnified examination of the vagina, the ectocervix as well as the cervical canal. Both the vaginal and ectocervical mucosa are lined with a non-keratinized stratified squamous epithelium and appear in a pale pinkish color. Unlike the ectocervix, the vaginal lining adjusts to the cavity by forming big foldings, vaginal wrinkles, until the fornix. To unfold the latter, a moderate distension is needed by a gentle obstruction of the vulvar orifice. The cervix is located at the vaginal dome and can display normal or abnormal features which are visible in hysteroscopy: mucus, ectropion, ectocervical polyps, cysts, adhesions and endometriosis implants, to name but a few (Fig 1-3).

The endocervical canal however is lined by a different mucosa consisting of a single layer of mucus-producing columnar cells, and hence appears more reddish. Among the frequently encountered lesions: Nabothian cysts, cervicitis, polyps and adhesions.

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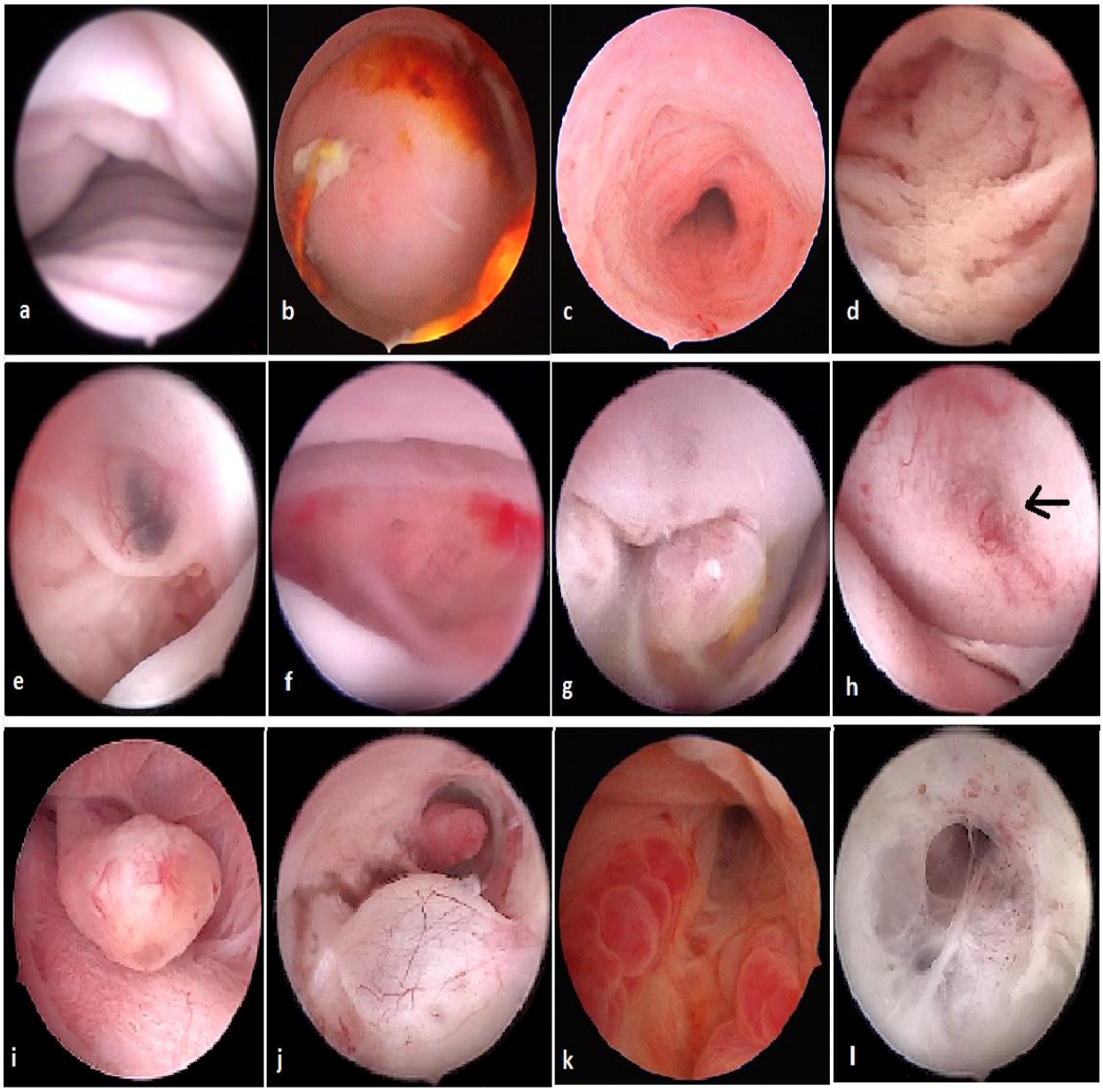

Figure 1. Vagina and cervix at standard diagnostic hysteroscopy. a) vaginal folds; b) ectocervix with mucus; c) cervical canal; d) detail of papillary structures (arbor vitae); e) ectocervical endometriosis; f) ectropion; g) endocervical polypoid papillae; h) total synechia of the external os of the cervix; i) endocervical polyp; j) Nabothian cyst with endocervical adhesions and polyp behind; k) endocervicitis; l): endocervical adhesions. (Images by A. Drizi)

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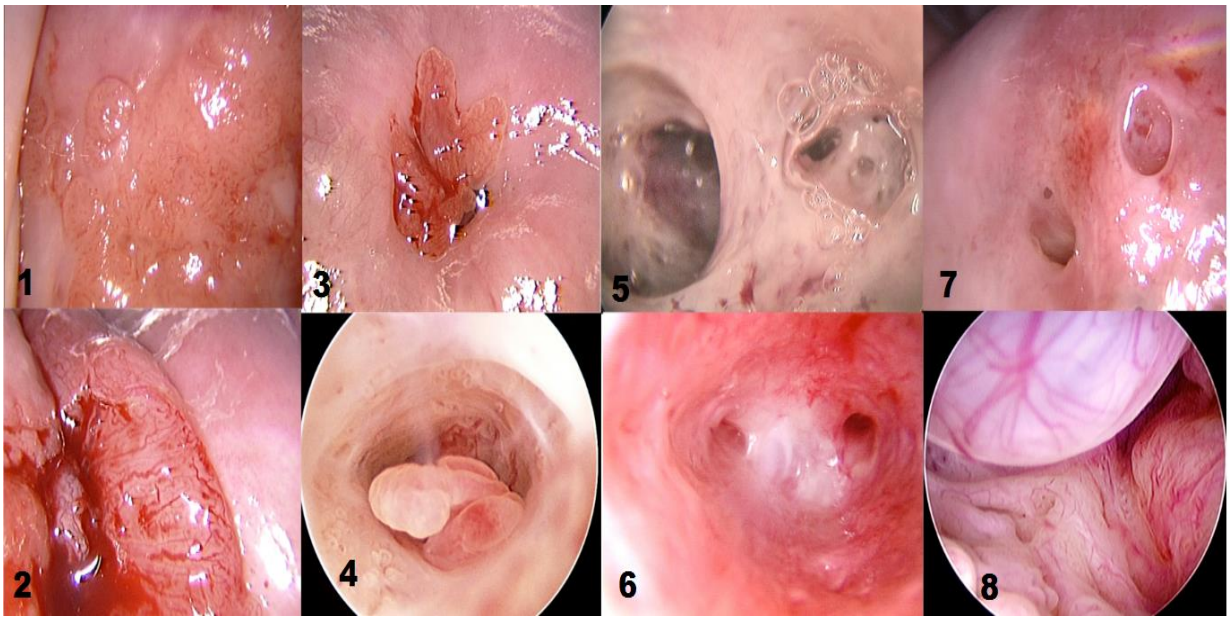

Figure 2. Various cervical lesions: 1) Cervical carcinoma; 2) Adenocarcinoma; 3) Small polyp protruding from external orifice 4: Endocervical polyp 5: Isthmic adhesions 6: Cervical adhesions 7: External orifice adhesions mimicking two orifices 8: Endocervical Nabothian cyst. (Images by L. Montevecchi)

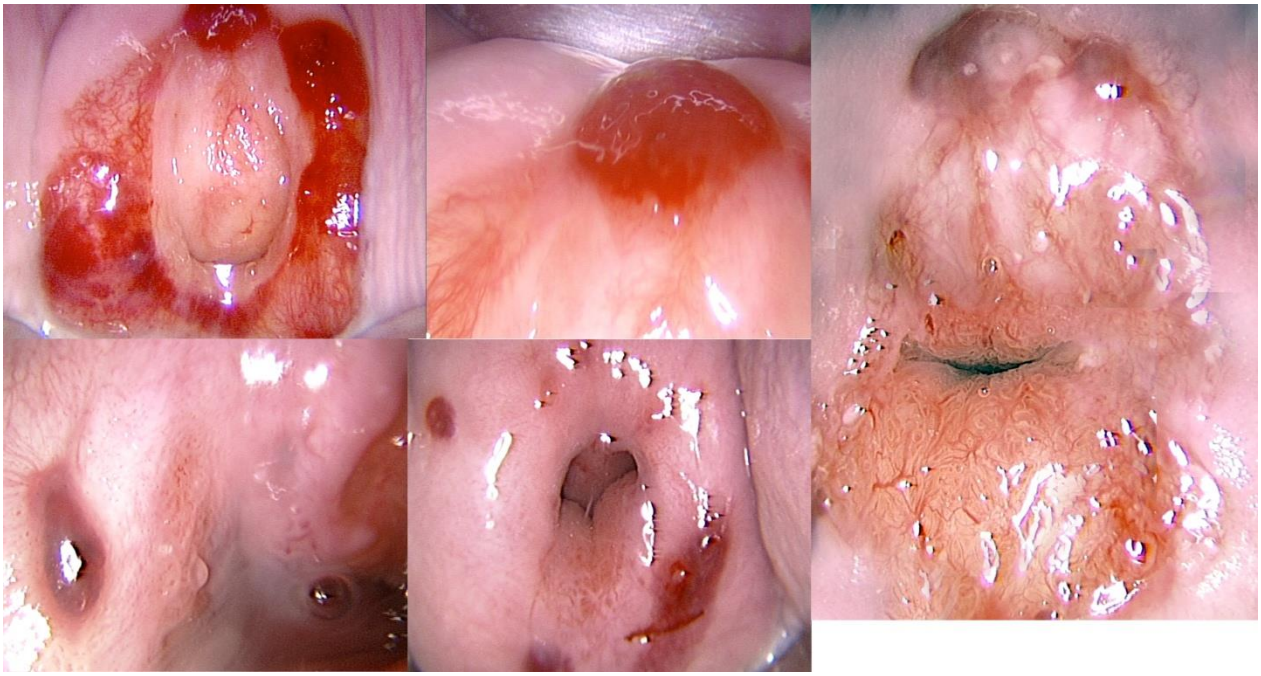

Figure 3. Different aspects of cervical endometriosis. (Images by L. Montevecchi)

Using the Hamou micro-colpo-hysteroscopy, instead of the normal hysteroscope, we can observe not only the vagina, the cervical canal and the uterine cavity, but also the "contact" vision of the epithelium up to 150 magnifications.

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The Waterman's blue ink (the common ink of fountain pens) can color the squamous epithelium of the uterine cervix and vagina "in vivo", thus allowing observation without the need to remove the cells and send them to the laboratory.

The first micro-colpo-hysteroscope sold in the world was purchased in 1981 by Luigi Montevecchi from Italy and allowed correlation studies between hysteroscopy and histopathology.

Over the past 42 years one of the authors (L.M.) has used, in sequence, the three Hamou micro-colpo-hysteroscopes models (type I, II and III) to observe the epithelium of the uterine cervix and vagina for the accurate diagnosis of lesions caused by the Human Papilloma Virus (HPV) (Fig.4).

After the original model, characterized by a double eyepiece and a button capable of diverting - thanks to the interposition of a mirror - the vision from the direct to the offset eyepiece, Hamou created a second model (type II) much more manageable, with only eyepiece that allowed magnification up to 80x. The focus knob (present either on the first model no longer in production, and on the two most recent) allows a permanent clear view at different focal lengths.

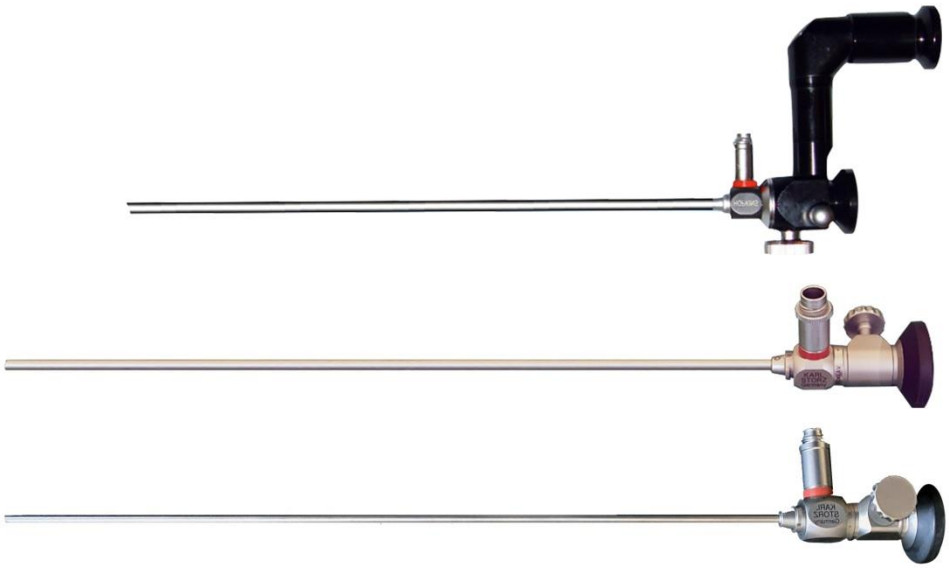

Figure 4. From up to down: types I, II and III Hamou microhysteroscopes, with a side focus knob for all models

The Type III differs from the Type II by the reduction of the caliber which goes from 4.5 to 2.7 mm.

It is necessary to have a light source with a fiber optic cable, and a high quality endo-camera to obtain an adequate view of the cellular elements on a large monitor.

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Materials and Method:

The technique of Microcolpohysteroscopy (MCH), already extensively described in previous publications, consists of exposing the uterine cervix with a common vaginal speculum (1-3). We then proceed to cleanse the surface of the epithelium with a cotton swab soaked in physiological solution, to remove the cervical mucus which can sometimes be very abundant. Lugol's iodine solution is then applied to assess the degree of maturity of the epithelium. The areas that capture the solution are those stimulated by estrogens, rich in glycogen, and capable of carrying out the normal functions of the mature squamous epithelium. Their color turns deep brown (Fig. 5)

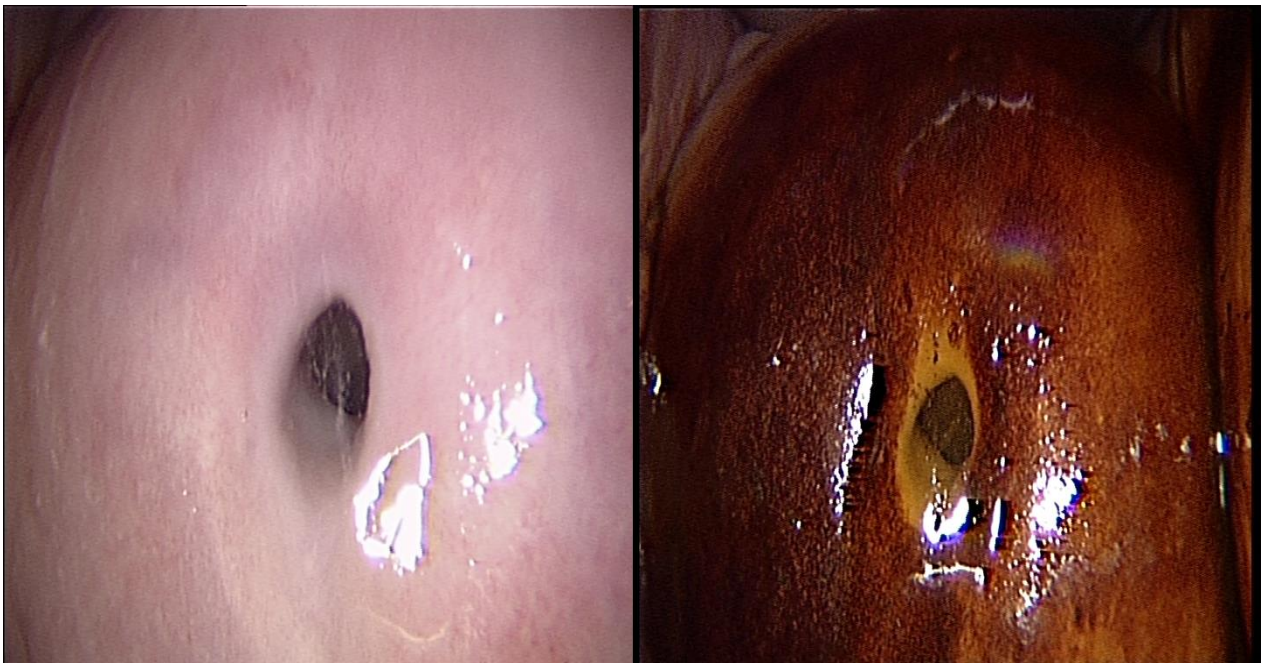

Figure 5. Normal uterine cervix before (left) and after (right) application of Lugol's solution. (Images by L. Montevecchi)

After this first superficial evaluation, the tissue is colored with Waterman's blue ink. It penetrates into the cytoplasm and the nucleus of the mature squamous epithelium, and into the one in squamous metaplasia (more or less mature), leaving the cylindrical epithelium colorless (Fig. 6). This feature allows an easy differentiation between squamous and cylindrical epithelium, making it easy to identify the squamous-cylindrical junction, so important for the study of pre-neoplastic lesions of the uterine cervix.

We collected most of the data in a digitized way, first on a Personal Computer (PC) with the "Access" database, then, starting from 2012, on a Mac platform with the FileMaker database.

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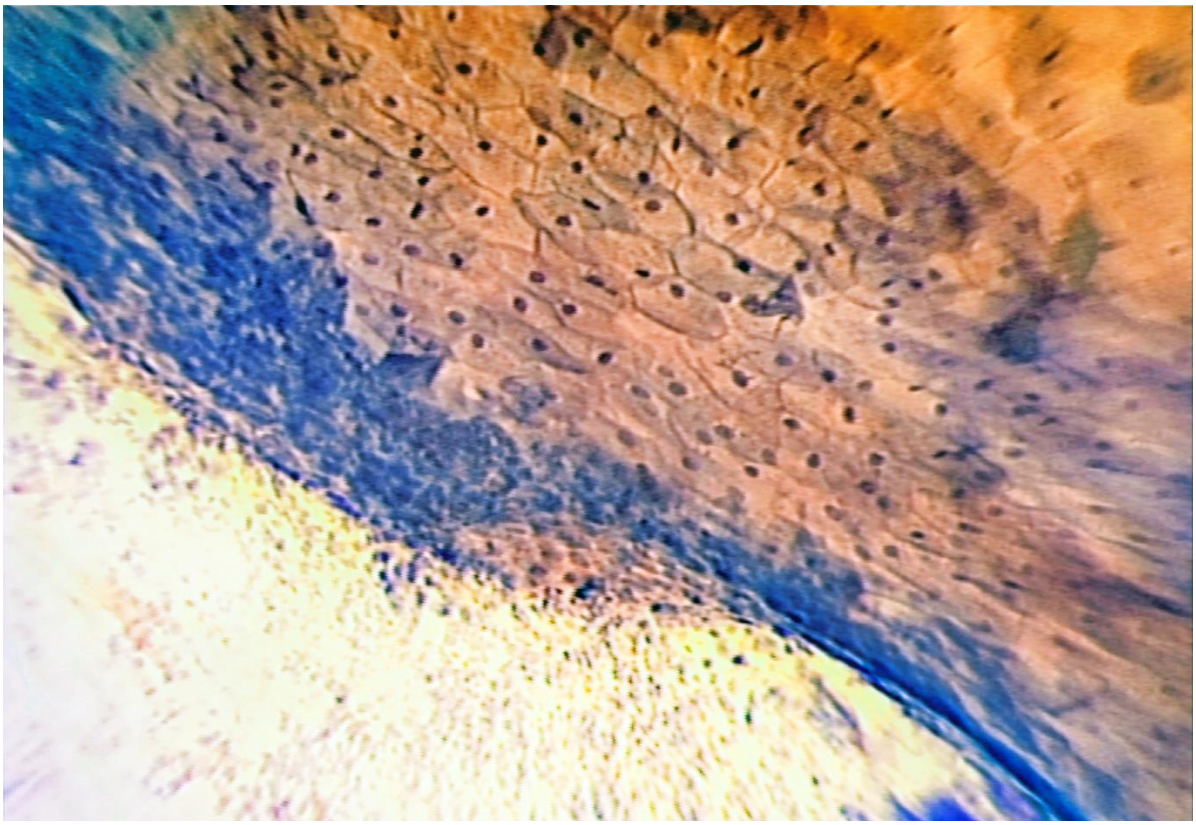

Figure 6. The squamo-columnar Junction (SCJ) (Microcolpohysteroscopy x150):
Bottom left: unstained cylindrical epithelium; top right: mature superficial squamous epithelium; blue cells: Transformation Zone (Images by L. Montevecchi)

After the first years, during which the MCH images were carefully compared with the results of the histological diagnosis deriving from the biopsy, we stopped carrying out a systematic check, having obtained an almost total correspondence between the MCH diagnosis and the corresponding cytohistological condition, more precisely than the traditional colposcopy and confirmed by flow cytometry (4-7).

Figures 7-9 document in a very precise way the morphological correspondence between normal squamous epithelium, cytopathic alterations from HPV and high-grade lesions (7-10), which allowed us to make an accurate diagnosis without the need to take biopsy samples for confirmation.

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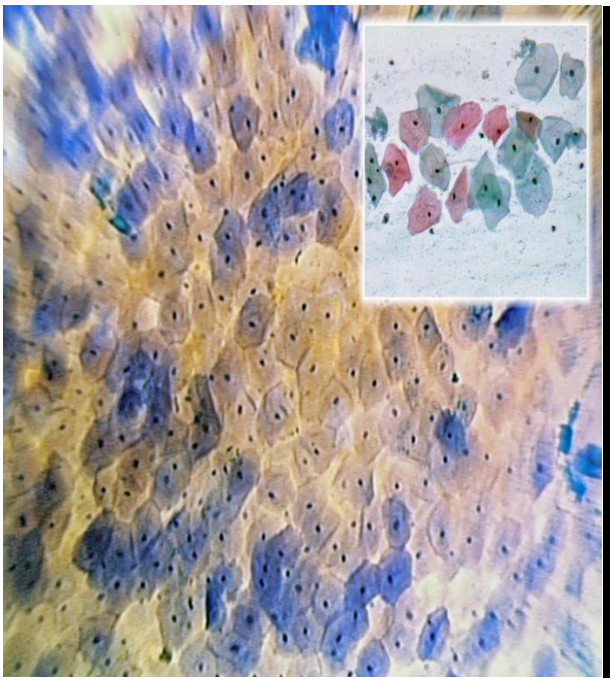

Figure 7. Normal Epithelium (Microcolpohysteroscopy x150): note the polygonal cells with a pyknotic nucleus regularly distributed on the surface of the epithelium (Inset: Cytology x250). Images by L. Montevecchi

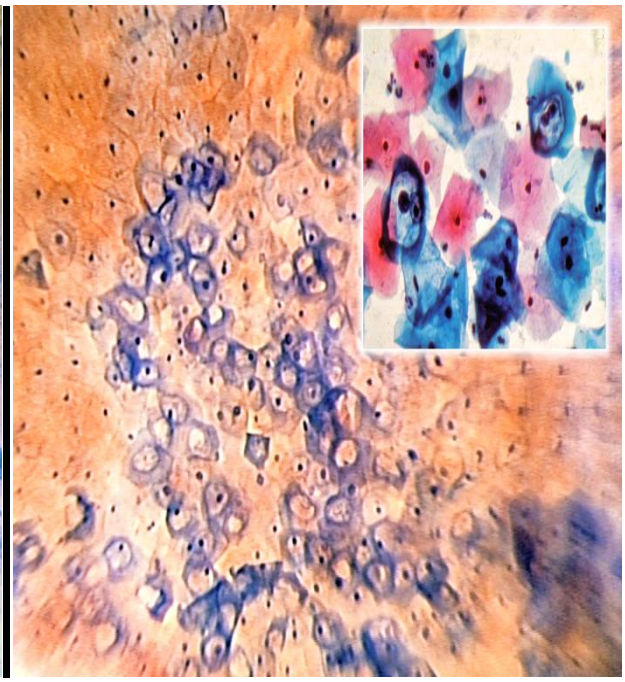

Figure 8. Koilocytosis (Microcolpohysteroscopy x150): rounded cells with hyperchromic nucleus and clear perinuclear cytoplasmic halo (Inset: Cytology x250). Images by L. Montevecchi.

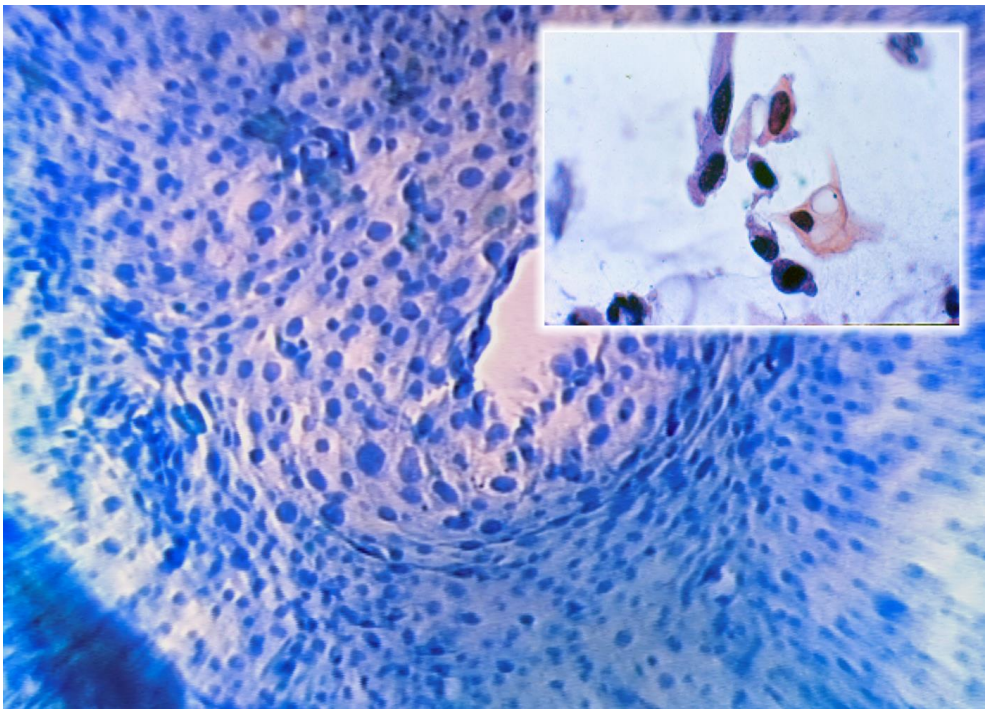

Figure 9. High Grade Lesion (Microcolpohysteroscopy x150): marked anisokaryosis, irregular cell distribution, altered nucleus/cytoplasmic ratio in favor of the nucleus with little cytoplasm (Inset: Cytology x250). Images by L. Montevecchi

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Results and Discussion

We reviewed 3056 consecutive MCHs performed from 2012 January 1st to 2022 December 31th (Mean age = 41; Median = 39; SD= 12). Some data are summarized in table 1 and Fig 10.

In 169 patients submitted to MCH with negative Pap smear (referred for examination for routine control or for positivity to the HPV DNA test) we diagnosed 81 subjects (48%) with cytopathic alterations caused by the Papillomavirus, not recognized by cytological examination.

Microcolpohysteroscopies 2012/2022

Years	# of MCH	Negative Cytology and Positive MCH	Positive HPV DNA and Negative MCH	HSIL
2012/2015	858	35	12	45
2016	269	6	12	8
2017	280	3	13	11
2018	349	10	24	27
2019	357	10	15	25
2020	298	3	18	15
2021	331	8	29	17
2022	314	6	22	14
Total	**3056**	**81**	**145**	**162**

Table 1. The main findings collected out of the 3056 microcolpohysteroscopy (MCH) procedures from 2012 to 2022. HPV: Human Papilloma Virus; DNA: Deoxyribonucleic Acid; HSIL: High grade squamous intraepithelial lesion.

This confirms some observations already published in old articles (2) and the reason is the more complete and precise examination of the entire uterine cervix, and of the Squamo-Columnar Junction (SCJ), made by MCH, in comparison with the cellular sample collected with the Ayre's spatula. In 145 cases out of 658 (22%), sent to MCH for positive Human Papilloma Virus (HPV) test (16, 18, 31, 33 or other Papillomaviruses) there were no cellular alterations referable to the presence of the HPV. This can be easily explained by remembering that the cellular modifications depend on two competing factors: the aggressiveness of the virus and the defense capabilities of the host organism. The presence of the virus, revealed by gene amplification on a swab, is not always capable

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of inducing cellular alterations detectable by microscopic observation (Fig. 10).

We have diagnosed or confirmed 162 cases of HSIL, identifying the location and extent of the lesions. Most of them have been referred to their own doctor for excisional treatment of the pathological areas. In 16 cases out of 162 we had a copy of the histological examination after conization. The correlation between MCH and histological diagnosis was 100%.

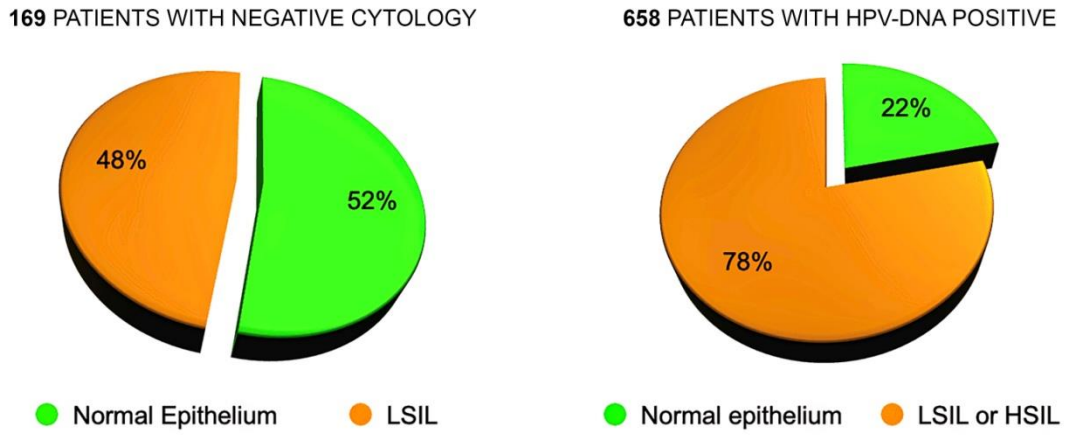

Figure 10. Discrepancy between Cytology, HPV-DNA Test and Microcolpohysteroscopy. HPV: Human Papilloma Virus; DNA: Deoxyribonucleic acid; HSIL: High grade squamous intraepithelial lesion; LSIL: Low grade squamous intraepithelial lesion.

Conclusion:

The vaginal approach to the uterine cavity using a liquid distension medium allows to observe normal and pathological aspects of the vagina and uterine cervix, under macroscopic magnification.

The microcolpohysteroscopy, performed with the Hamou microcolpohysteroscope, allows immediate observation of the cells lining the vagina and the uterine cervix, without the need to perform a biopsy and wait for the result of the histology.

It allows, in a single session, to determine the presence of a lesion, to evaluate its severity, location and extension and to decide whether to repeat the examination after some time, or to perform a treatment, knowing in advance the location and extent of the lesion.

Compared to cytology, it allows identification of the position and extent of altered cells, and eliminates the interval between sampling and the laboratory response.

Compared to colposcopy, it allows precise determination of the internal limit of the lesion even in the case of unsatisfactory colposcopy, so as to obtain a customized surgical removal and reduce the risk of excessive or insufficient

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excisional treatment (12).

Compared to the HPV DNA test – which can only ascertain if a high-risk virus is present or not – it can verify whether - whatever the type of HPV present - it has already been able to induce cellular alterations, and of what degree.

Although the term hysteroscopy etymologically indicates examination of the uterus, more can be screened thanks to this technology, including the vagina and the cervix.

Microcolpohysteroscopy, in addition to standard hysteroscopy, allows an excellent in vivo examination of cells which this study has confirmed.

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Diagnostic hysteroscopy: an atlas-like review of the endometrium from normal to malignant

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The author declares no conflicts of interest

Abstract

Reporting a normal endometrium during a diagnostic hysteroscopy needs to be based on objective criteria taking into consideration the histological, physiological and pathological features of the mucosa. The evaluation can be challenging because of the cyclically changing character of the mucosa, displaying different features depending on the subphase of the menstrual cycle.

In this article, an atlas-like overview from a purely diagnostic perspective of the main features of the endometrium is provided with the main educational objective of facilitating the interpretation of the hysteroscopic images of the endometrium in a way which is based on fundamentals. The targeted states are normal, dysfunctional/inflammatory, adenomyotic, polypoid, hyperplastic and malignant endometria. The general principles of sampling and writing the descriptive report are further discussed. The assessment of endometrial vascularization is excluded as it is the subject of a different article in this special edition.

Key words: normal endometrium; dysfunctional inflammatory endometrium; adenomyosis; endometrial polyps; hyperplasia and malignancies; sampling and descriptive report.

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Introduction:

The endometrium is the mucosa lining the uterine cavity, on top of the myometrium. The first concern of a hysteroscopist during a diagnostic procedure is to distinguish normal from abnormal, as this separation results in medical-legal consequences. Defining the normal endometrium is relatively complex as it is a cyclically-changing mucosa, with different aspects depending on the phase, and even at times on the subphase of the menstrual cycle. Consequently, no pertinent examination can be conducted in the ignorance of the basic sciences related to endometrial histology and by extension, physiology and pathology.

In this article presented in the form of an atlas, the main objective is to provide an educational simplified review of the endometrium in its different patterns: normal, dysfunctional, inflammatory, polypoid, hyperplastic and malignant, taking into consideration the available evidence of the literature.

Normal endometrium – a cyclically changing mucosa.

Regardless of the phase of the menstrual cycle, the global architecture of the endometrium remains the same, as it is composed of a surface epithelium which folds into perpendicular glands invaginating into the underlying stoma (1). The latter supports the regularly spaced endometrial glands and consists of a connective tissue where stromal cells and blood vessels fill in the interglandular spaces (fig 1). Moreover, the thickness of the mucosa contains two functionally distinct layers. The superficial one termed the functionalis is the one repeatedly shed during menses or, in case of pregnancy, the site of the embryo implantation. The basalis is the deeper layer whose role has always been postulated to permit regeneration of the shed functionalis. Recent studies revealed a horizontal network of gland rearrangements in the basalis in contrast to their vertical disposition in the functionalis (2) (fig 1). This complex horizontal network of mycelium-like interconnected glands was demonstrated to contain endometrial stem cells giving rise to the functionalis glands. This new disposition additionally explains the horizontal spread of stem cells thus allowing self-renewal of the entire endometrial glandular elements at an adjacent deficient region (2).

Because the single-layer surface epithelium is transparent, examination of the normal endometrium by hysteroscopy only reveals the pinkish underlying stroma with the perpendicular glands, appearing as evenly distributed white dots, surrounded by blood vessels in places (fig 1C).

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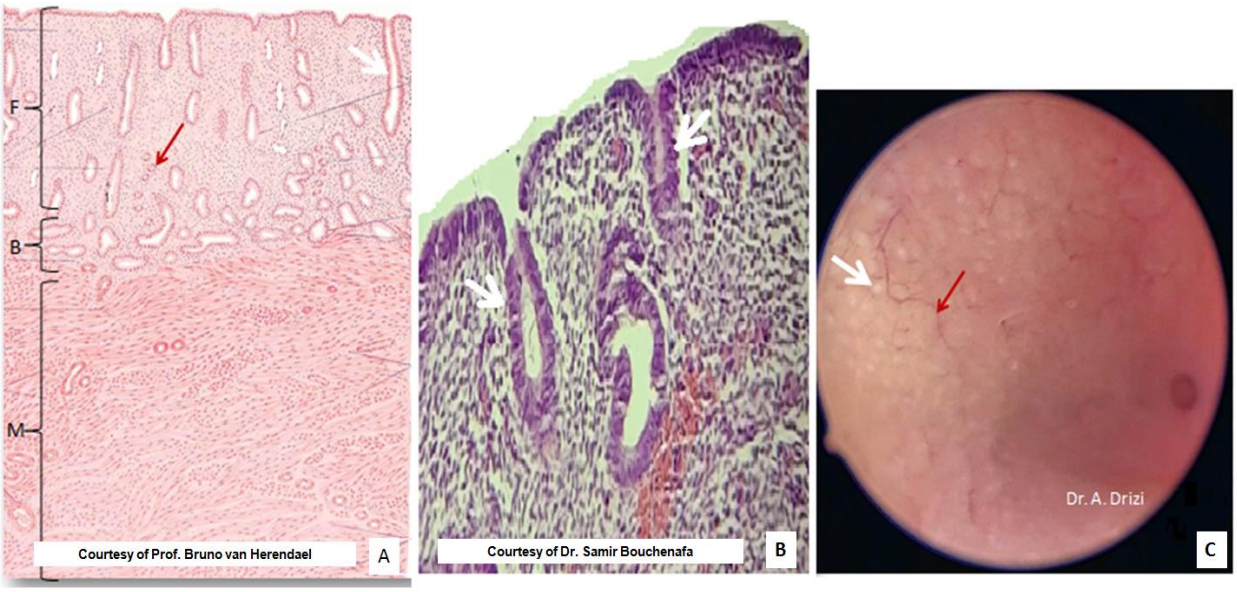

Figure 1. General features of normal endometrium. A: at histology, with the functionalis (F), the basalis (B) where glands are horizontal and the myometrium (M). B: at hysteroscopy. White arrows: endometrial glands; red arrows: endometrial vessels; stromal cells fill the spaces between glands and vessels.

The above cited common features of the endometrium display changes throughout the menstrual cycle depending on the given phase (follicular and luteal) and sometimes even the subphase (early, mid and late proliferative or luteal) (1, 3). A description of the endometrium at the different phases of the menstrual cycle was published in a handout in early 2022 (4). Moreover, the main characteristics of the proliferative endometrium were described in details both histologically and hysteroscopically in a recent review article (3) and are summarized in Table 1.

Although hysteroscopy can also be performed during luteal phase, the proliferative phase was more targeted as it avoids the physiological thickening of the mucosa and increased cervical tonicity caused by the post-ovulatory hormonal environment (3).

Growing awareness of the normal and pathological features of the endometrium is of utmost importance for a proper hysteroscopic examination of the mucosa and also for a thoughtful interpretation of the pathologist's report.

Among the common features of normal endometrium are the growing thickness of the mucosa throughout the menstrual cycle, the regular distribution of endometrial glands (figures 2, 3) and vessels. The stromal edema is a physiological finding during mid proliferative phase and luteal phase (1, 3, 5).

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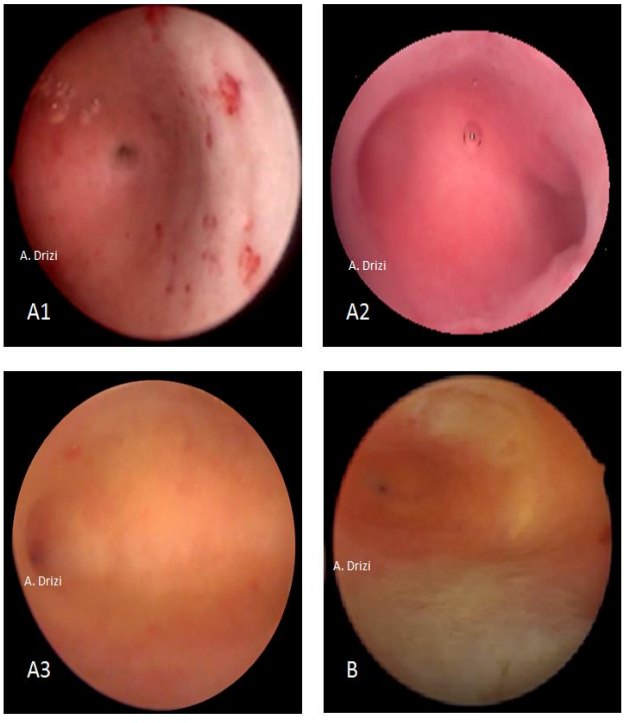
Histological and physiological features	**Early proliferative Days 5-7/28**	**Mid proliferative phase Days 8-10/28**	**Late proliferative phase Days 11-14/28**	**Secretory phase Days >15/28**
Thickness	Flat epithelium Thin endometrium	Higher endometrium	Slightly less thick endometrium	Day by day changes (excluded)
Glands : regularly spaced+++	Sparse, narrow, and straight glands	More numerous glands. Beginning of tortuosity	Marked tortuosity of glands	/
Epithelial cells	Cuboid or low columnar cells	Tall columnar cells. No pseudostratification	Pseudostratifi-cation	/
Stroma	Loose stroma of spindle-shaped cells	Interstitial edema	Interstitial edema subsided	/

Table 1: the cyclical changes in proliferative phase (vessels excluded).



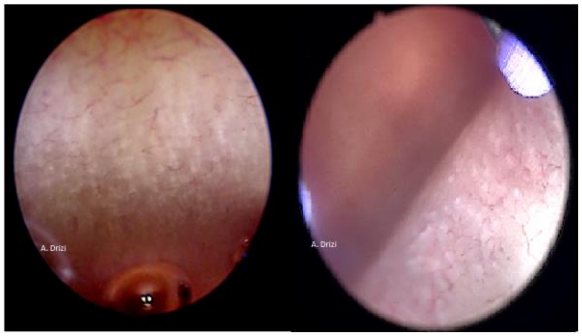


Figure 3. Regular distribution of endometrial glands during proliferative phase.

Figure 2. . Diagnostic hysteroscopy of normal endometrium at the different phases of the menstrual cycle. A: proliferative phase; 1: early proliferative (thin disorganized, few gland orifices and petechiae); 2: mid proliferative (thicker, pinkish with physiological edema); 3: late proliferative (slightly less thick due to subsided edema, yellowish-pinkish color). B: luteal phase (much thicker, edema, mucosal foldings).

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Although the endometrium is known to be a hormone-responsive mucosa, it is already well established in anatomopathology that the basalis and the isthmic mucosa are poorly responsive to hormones and hence cannot allow proper dating when sampled (6,7). Consequently, dating requires to avoid sampling within the isthmic region, hysteroscopically identifiable thanks to its anatomical landmarks which have been described by the anatomists in 1905, and at hysteroscopy in 2020 (8). The limits are the internal histological uterine os –commonly known as the internal os of the cervix– and the internal anatomical uterine os, located 6 to 10 mm above the first one (fig 4).

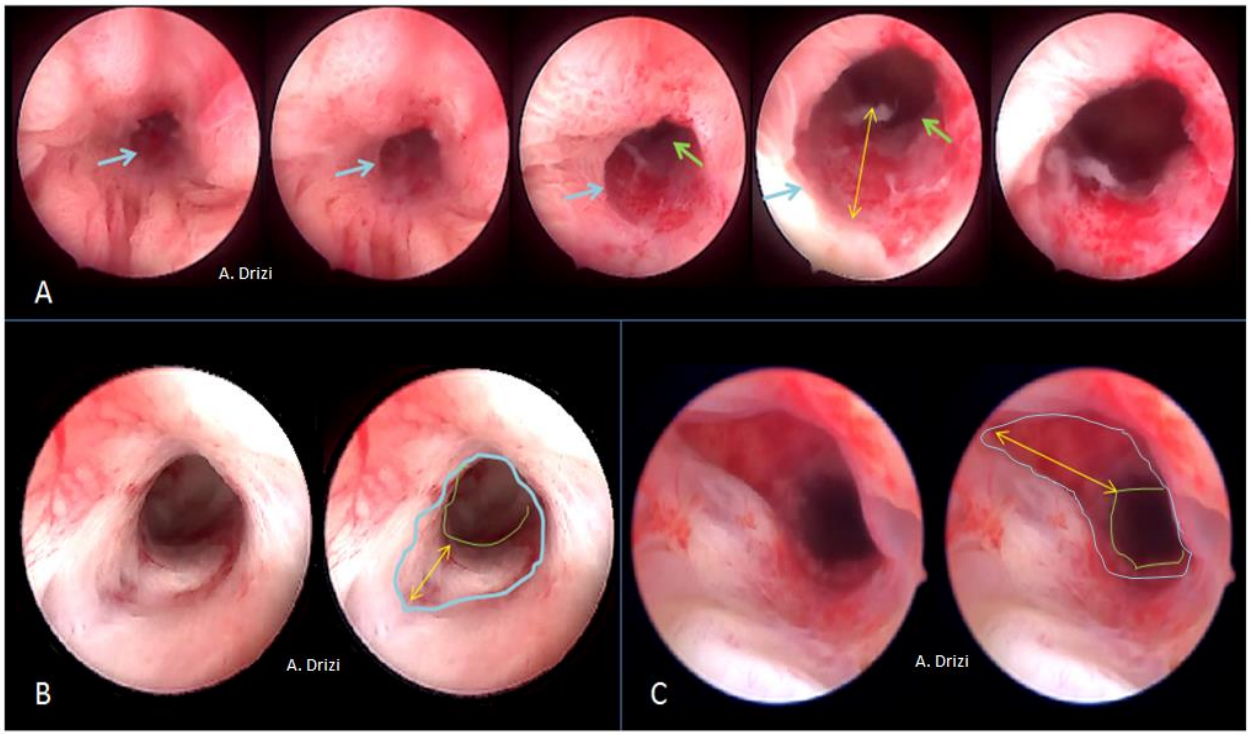

Figure 4. Uterine isthmus at hysteroscopy. A: nulliparous woman: from the cervix to the cavity; B: post-menopausal woman; C: multiparous woman. Blue: histological internal os of the uterus; green: anatomical internal os of the uterus; Yellow arrow: length of the isthmus.

In post-menopausal patients and with the arrest of the cyclical hormonal activity, the endometrium enters into a chronic state of inactivity, consisting of a thin atrophic mucosa with scarce glands, sometimes dilated thus defining cystic atrophy (1, 6). The thinning of the mucosa can be so important that the marks of the underlying circular muscular fibers of the myometrium become visible (fig 5). Endometrial atrophy is also observed in breastfeeding women and in patients under chronic thinning hormone context (hyperprolactinemia, progesterone therapy, tamoxifen, to name just a few).

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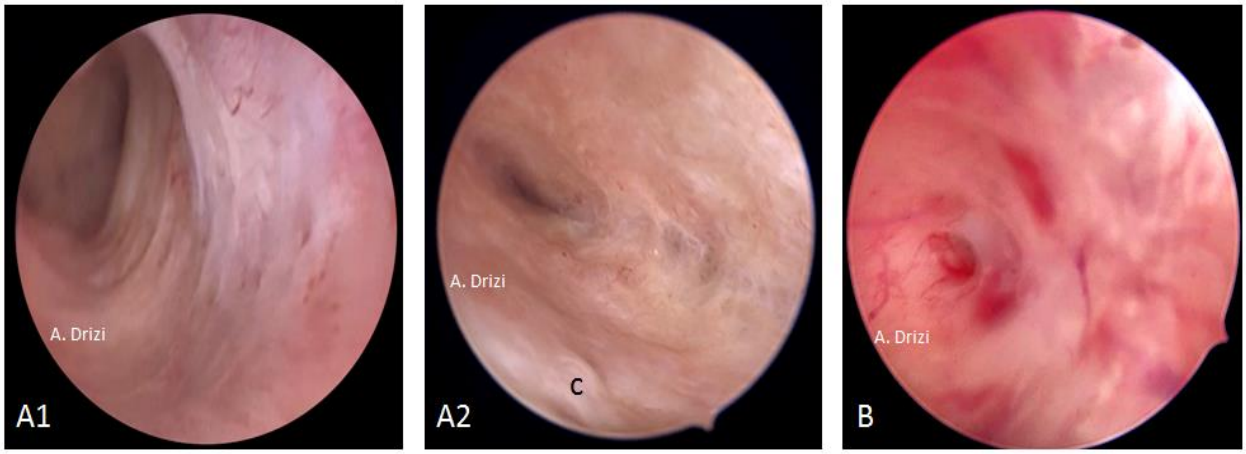

Figure 5. Endometrial atrophy. A: in post-menopausal women; 1: visible marks of the underlying circular muscular fibers of the myometrium due to advanced atrophy; 2: closer view: scarce glands, cystic in places (c); B: scarce atrophic glands and heterogenous vascularization with Mirena.

Dysfunctional inflammatory endometrium.

The term dysfunctional etymologically designates perturbed functions of an otherwise organically normal structure. In the case of the endometrium, dysfunctional has long been exclusively associated with hormone imbalances, however there is a significant amount of literature linking hormone disorders to the broad spectrum of inflammation (3, 5, 9).

Unlike the common thinking in gynecology, inflammation is a normal component of the endometrial physiology and its impairment cannot be exclusively limited to microbial aggressions but to whatever disrupts homeostasis, such as allergens, oxidative factors, pollution, metabolic imbalances, adenomyosis, endometriosis as well as hormone imbalances to name just a few, resulting in an impaired inflammatory state of the endometrium (IISE) (10).

For the functionalis to shed during menses, the physiological endometrial inflammatory cells (mainly Natural Killer cells NKc) free their cytotoxic contents, along with the predecidual cells, under the effect of progesterone withdrawal at the end of the menstrual cycle. In fact, both progesterone and estrogens have already been established to have anti-inflammatory properties on the endometrium (10). The rise of estrogens in the beginning of the menstrual phase contributes to the self-limiting inflammatory destructive process caused by menses and subsequently, allows regeneration of the endometrium whose glands and stroma develop; and whose height progressively increases (11, 12). Consequently, not only ovarian impairment of sex hormones does

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impact these functions, but all the pro-inflammatory factors interfering with the endometrial inflammation as well, since excessive inflammation has already been demonstrated to impact the endometrium's receptivity to normally-secreted ovarian hormones, thus resulting in a vicious circle (13). This explains how dysfunctional and inflammatory consist of two faces of a single coin, as they are closely interrelated (5, 13). This explains why, the presence of dysfunctional areas of endometrium in the entity chronic endometritis has been documented since the beginning of the past century and still to date (14).

These fundamentals need to be considered in our understanding and approach to dysfunctional inflammatory endometrium, to which the current definition of chronic endometritis does not do justice, hence the necessity to revise the current definitions or to propose more pertinent terminologies such as IISE or dysfunctional inflammatory endometrium (3, 10).

For a chronic IISE to cause clinical disorders (such as subfertility and recurrent miscarriage), stromal and/or glandular changes within the mucosa have already been presented necessary for the diagnosis by pathologists and physiologists, to such a point that their absence could ascertain the needlessness of a systematic search for plasma cells in the first place (7, 9). In fact, many pathologists agree that the diagnosis of chronic IISE should not rest on the unique finding of plasma cells in an endometrium that otherwise appears normal, because the background pattern is as important as the quantity of plasma cells (9, 14).

Among the hysteroscopic features of dysfunctional endometrium which can be correlated with histopathology are observed the commonly known signs for inflammation (15) (fig 6) as well as others which are overlooked and whose importance has been highlighted in a recent review (3).

The classic signs of chronic inflammatory endometrium are micropolyps, strawberry aspect, stromal edema, hyperemia and hemorrhagic spots (fig 6). The specificity and sensitivity is lower for the last three signs, as these are also the classic cardinal signs for acute inflammation as well (3).

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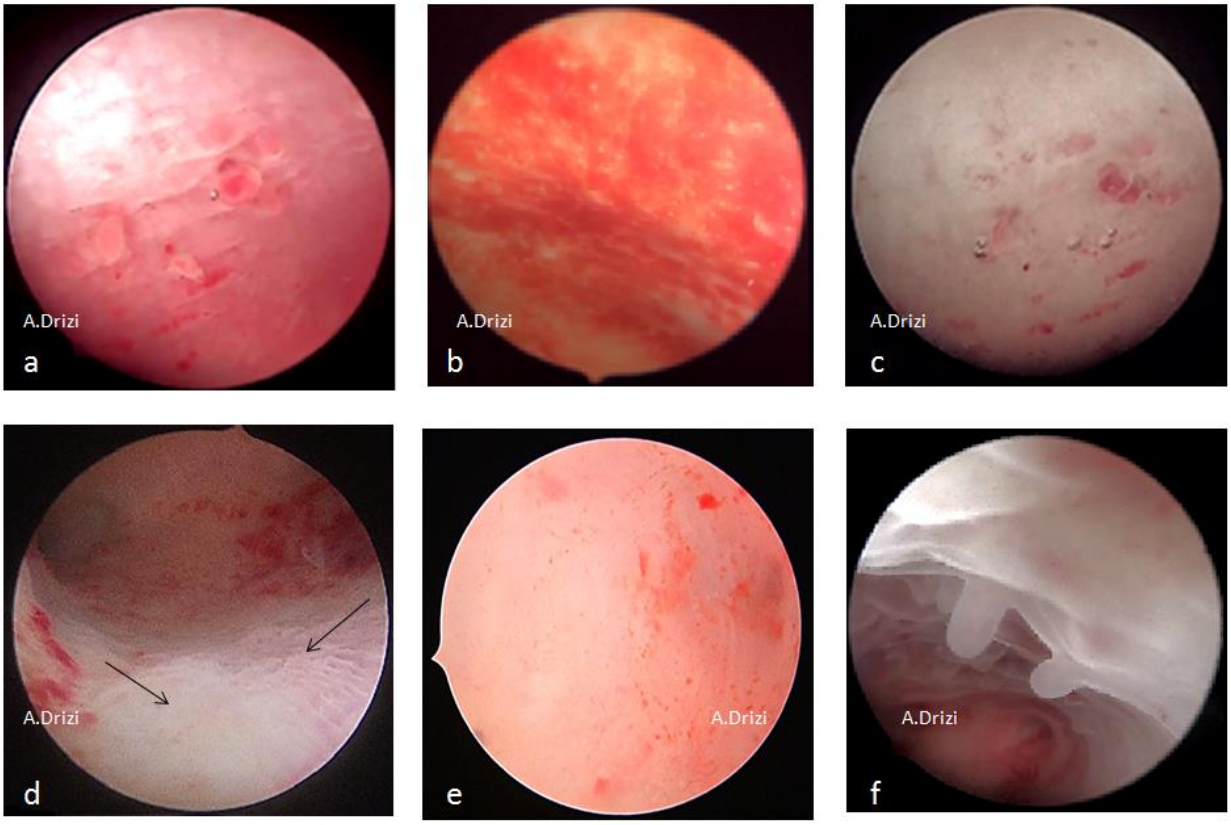

Figure 6. Classical acknowledged signs for endometrial inflammation. a: micropolyps; b: strawberry aspect; c: hyperemia; d: stromal edema; e: hemorrhagic spots; f: micropolyps with stromal edema and hyperemia in the fundus.

However, other hysteroscopic signs are overlooked although they are suggestive of a dysfunctional endometrium and hence are interesting to study as sampling sites (3). These additional signs are the irregular distribution of glands as well as the heterogeneous thickness of the endometrium, resulting in corrugated surfaces with embossed and debossed patterns (fig 7). In addition to stromal edema and endometrial hyperplasia, these aspects can be correlated with focal atrophic, deficient or resting endometrium; stromal breakdown and irregular proliferation, the latter being the dysfunctional disorder a stage below hyperplasia (3). Unevenly distributed glands are typically present in the strawberry aspect and in actual fact, all the above-mentioned signs can be associated with one another (3). In all cases, it is very important to be careful to these subtle aspects while performing a diagnostic hysteroscopy to optimize the sampling within the areas displaying these anomalies (fig 8).

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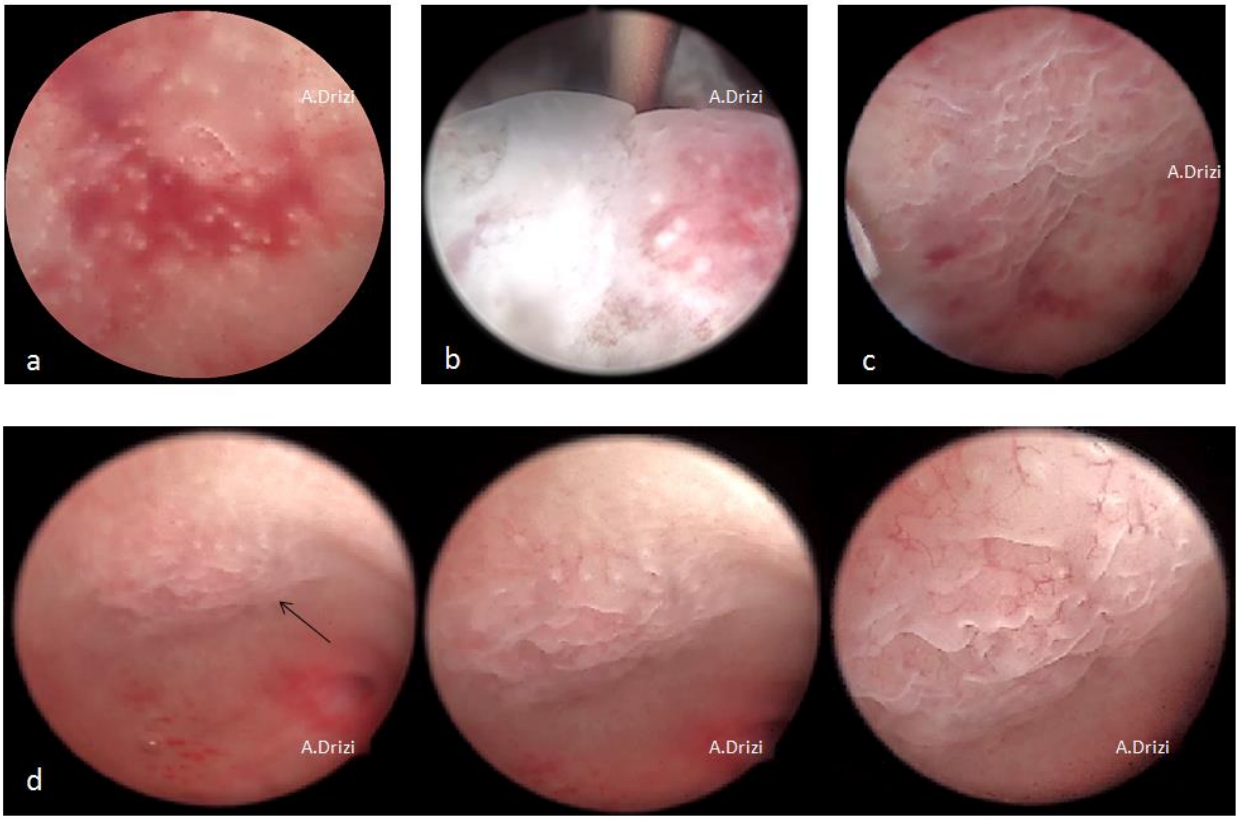

Figure 7. Additional signs for dysfunctional inflammatory endometrium: irregular distance between gland orifices associated with: a: strawberry aspect; b: edema (on the left) and hyperemia (on the right); c: corrugated irregularly thick area with embossed and debossed patterns; d: a subtle focally thickened mucosa showing typically corrugated surface at increased magnification (embossed and debossed patterns).

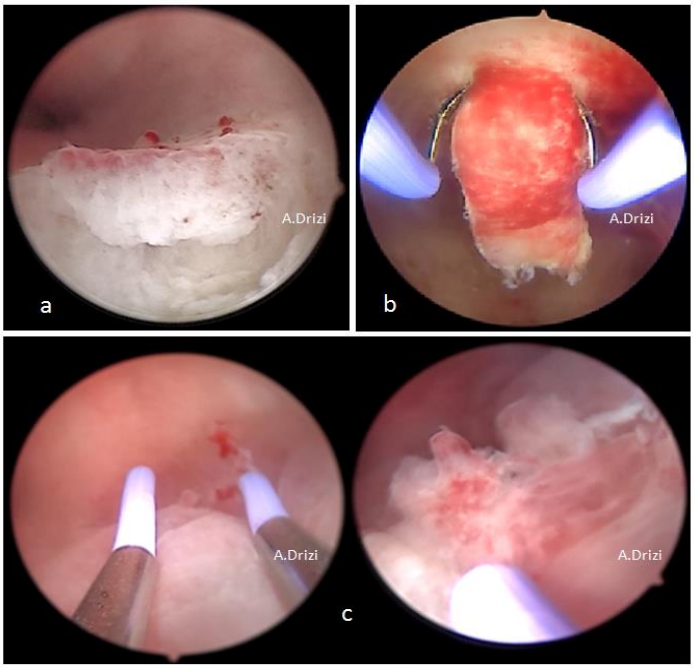

Figure 8. Targeted sampling performed within the endometrial areas displaying dysfunctional signs: a: micropolyps and hyperemia; b: strawberry pattern (with the loop); micropolyp+ irregular thickness and gland distribution (with the loop).

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Adenomyosis.

Among the chronic inflammatory diseases affecting women, adenomyosis is defined as the benign condition where active (hence inflammatory) endometrial glands and/or stroma are present within the myometrium. Among the common symptoms of the disease, heavy menstrual bleeding, secondary and/or aggravated dysmenorrhea, pelvic pain, subfertility as well as a higher risk of miscarriage/obstetrical complications have been reported (16). Imaging technology has provided consensual sonographic criteria suggestive of Adenomyosis by the Morphological Uterus Sonographic Assessment (MUSA) group (17), summarized in figure 9.

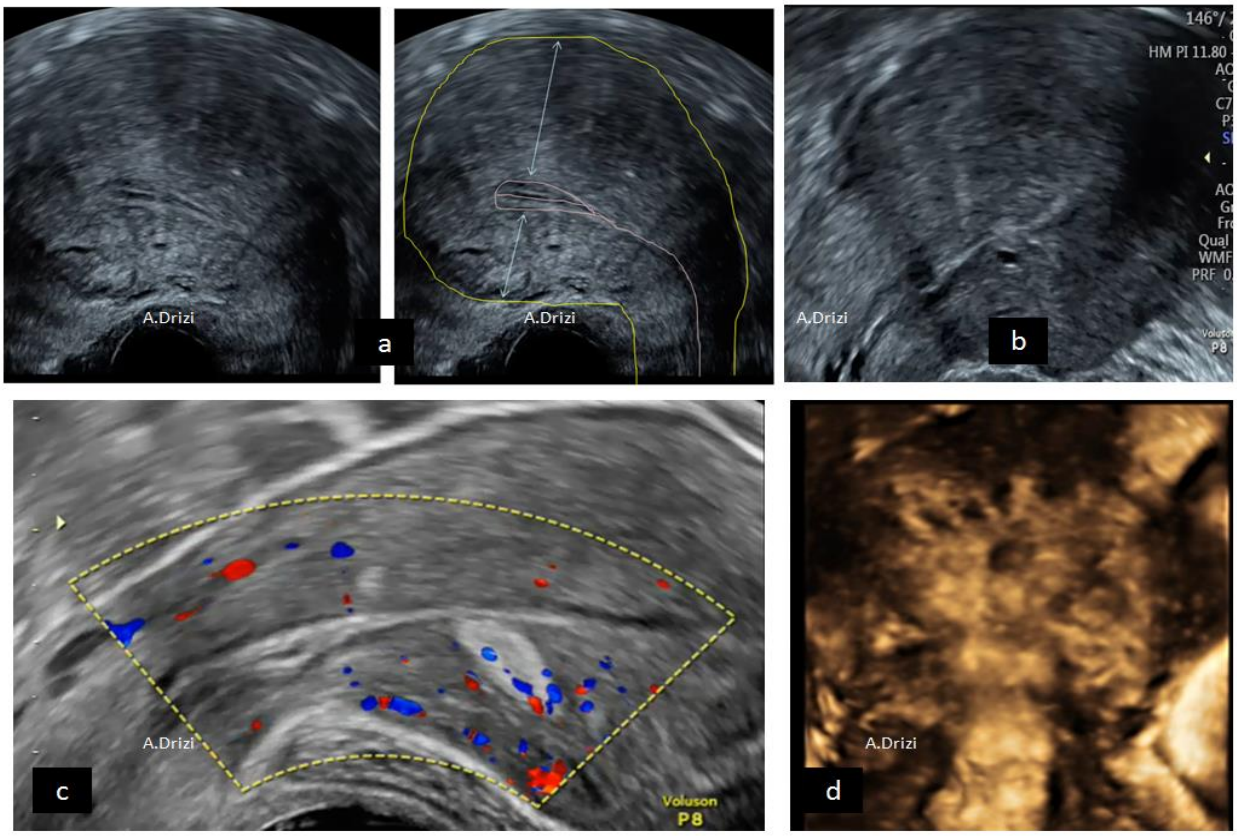

Figure 9. Ultrasonographic criteria of adenomyosis by the MUSA group: a: asymmetrical thickening, fan-shaped shadowing; b: cysts, subendometrial buds and lines; c: hyperechoic island, trans-lesional vascularity; d: irregular junctional zone.

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Although their pathognomonic character still remains to be proven, the following hysteroscopic signs are well accepted for adenomyosis and do more or so reflect the previously mentioned signs for dysfunctional inflammatory endometrium (fig 10): heterogeneous endometrial thickness with areas of focal defects (debossed patterns); submucosal hemorrhagic cysts displaying a dark blue or a chocolate brown appearance; fibrous cystic appearance of intrauterine lesions as well as hyper-vascularization (18, 19).

Figure 10. Consensually accepted signs for adenomyosis. a: debossed patterns: focal defect in atrophic endometrium; b: focal defect surrounded by strawberry aspect; c:fibrous cystic appearance of intrauterine lesions; d: hypervascularity; e: submucosal hemorrhagic cyst displaying a blue color, releasing a chocolate brown fluid after incision.

Endometrial polyps.

An endometrial polyp (EP) is a focal overgrowth of endometrial glands and stroma classically thought of as a hormone-mediated condition in spite of the increasing evidence on the role of chronic IISE in generating it (10, 20). Although it is typically a benign anatomo-clinical entity, the prevalence of malignancy may range from 1 to 3%, particularly in post-menopausal patients (10). Many patients can be asymptomatic, however among the common symptoms of the disease are abnormal uterine bleeding (AUB), subfertility and pregnancy loss (21).

From a diagnostic perspective, ultrasound provides accurate definitions especially when combined with saline/gel infusion sonography

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(SIS) (22). The typical sonographic features of an EP are a hyperechoic image characterized by the presence of a unique feeding vascular pedicle (22). The number, size, implantation base and location can also be defined by 2D, 3D and SIS.

Consequently and as the diagnosis of EPs is accurately defined by imaging techniques, diagnostic hysteroscopy is to be scheduled only before operative hysteroscopy begins and aims at providing a confirmation as well as a more accurate description of the features which cannot be assessed by ultrasound such as surface color and micro vascularization. The most accepted classifications of EPs are related to their macroscopic aspects, which can be pedunculated or sessile, single or multiple, ranging from millimeters to centimeters, located in the fundus in more than 50% of cases (21) (fig 11).

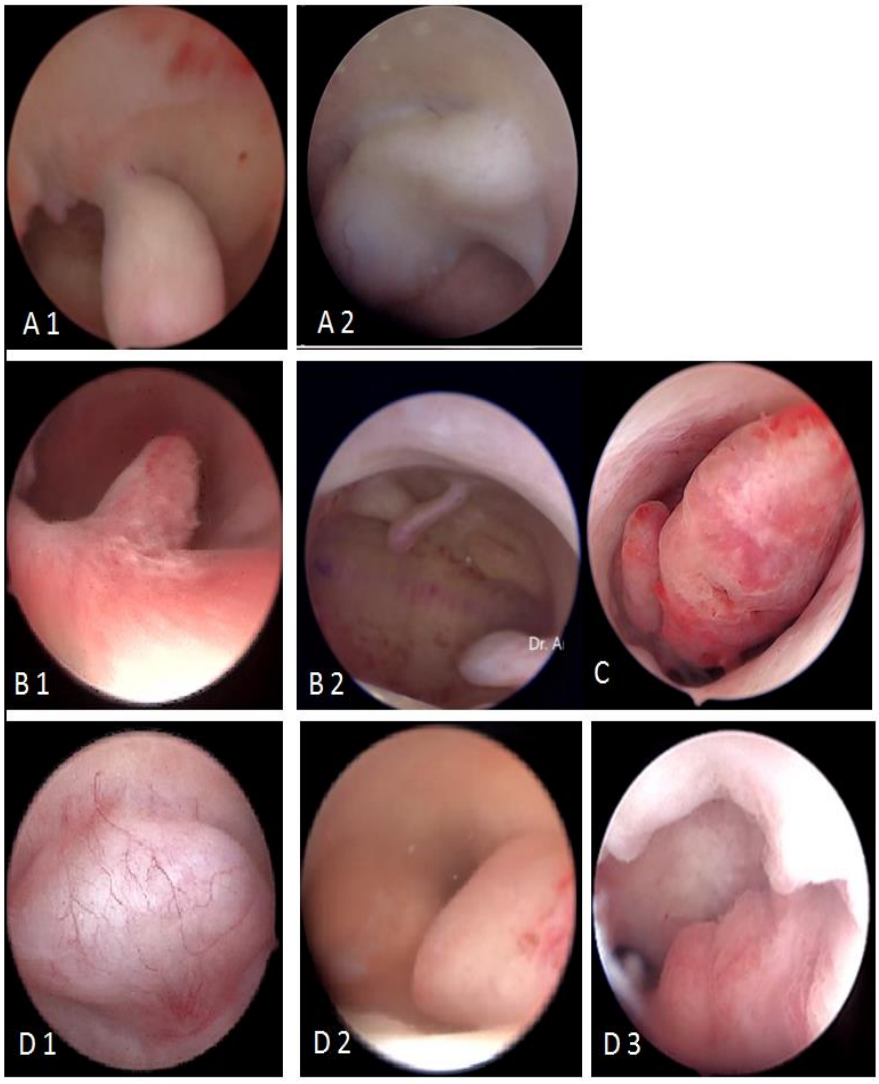

Figure 11. Macroscopic classification of polyps: A: pedunculated(1) or sessile (2); B: single (1) or multiple (2); C: various dimensions from millimeters to centimeters; D: various locations: fundus (1), corporeal (2) or isthmic (3). Images by A. Drizi

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The histopathological classification separates pseudo polyps –which are physiologically and temporarily observed during luteal phase – from hyperplastic EPs which can contain atypia in places. The other classes are functional (disappear under hormone therapy); atrophic (especially in menopausal women) and adenomatous EPs. The latter additionally contain smooth and fibrous muscle tissue (21) (fig 12).

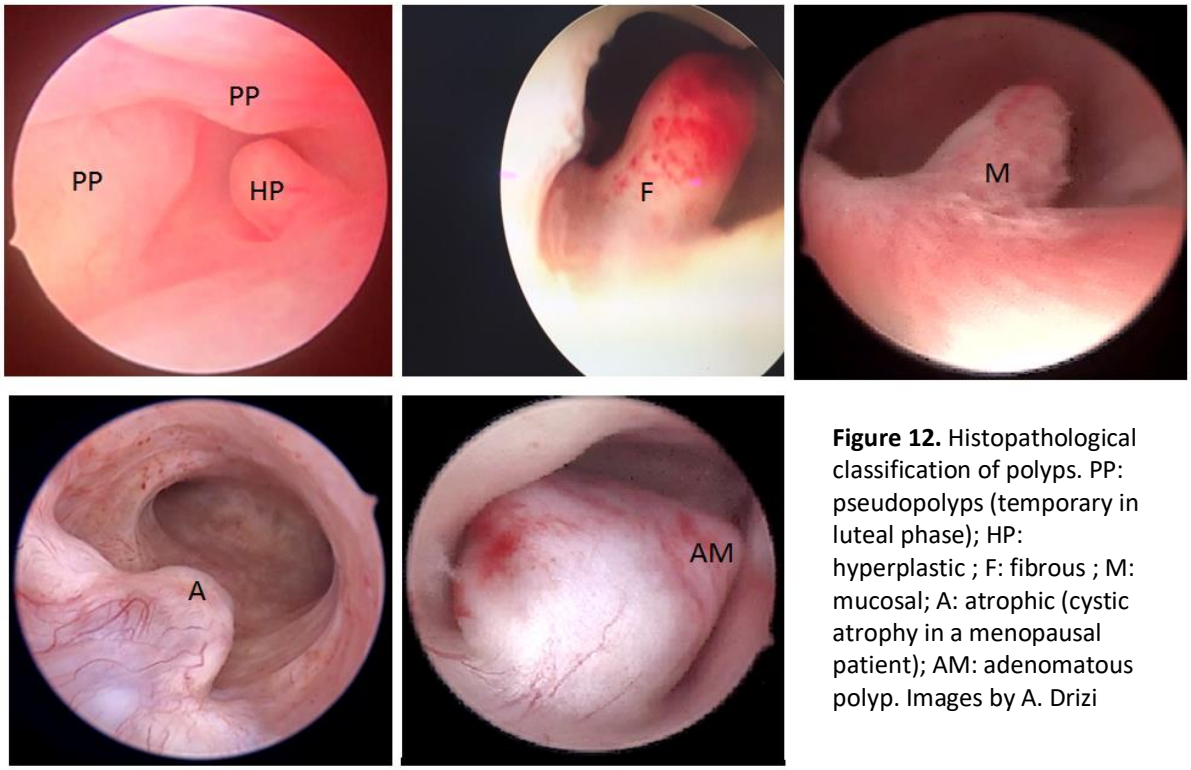

Figure 12. Histopathological classification of polyps. PP: pseudopolyps (temporary in luteal phase); HP: hyperplastic ; F: fibrous ; M: mucosal; A: atrophic (cystic atrophy in a menopausal patient); AM: adenomatous polyp. Images by A. Drizi

In addition to these histological types of EPs, others are encountered in our practice such as hemorrhagic and necrotic polyps displaying a blood-like color for the first and yellowish color for the second (fig 13). In all cases, the presence of a unique vascular pedicle is a sine qua none condition to define an EP at histopathology, which is commonly found at ultrasound but rarely seen in hysteroscopy (fig 13). However, the surface vascularity is always thin and regular.

The endometrium covering the EP has to be compared to the one lining the rest of the cavity. Other intrauterine pathology can be associated and if so will have to be reported.

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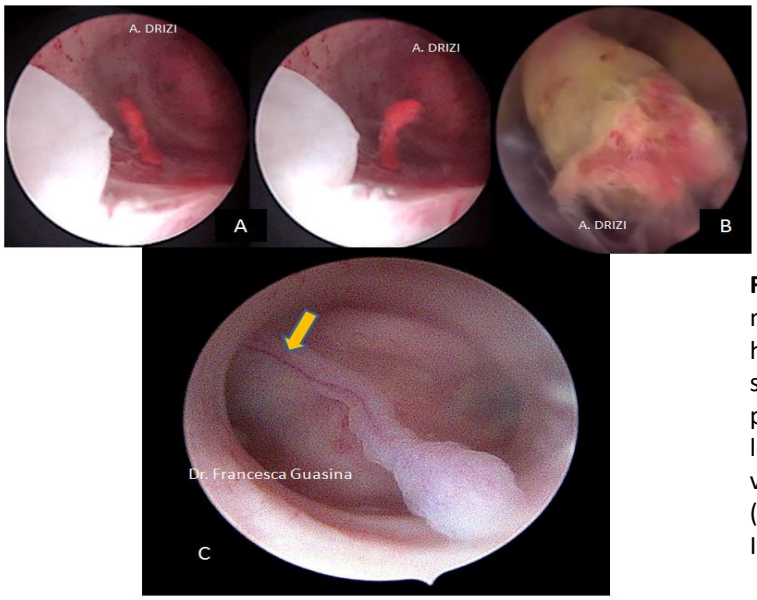

Figure 13. Other types of polyps usually not mentioned in classifications. A: hemorrhagic polyp (massive stromal suffusion of red blood cells); B: necrotic polyp (significant necrosis, yellowish); C: long pedunculated polyp with a unique vascular pedicle seen at hysteroscopy (Courtesy Dr. Francesca Guasina from Italy)

Endometrial hyperplasia and malignancy.

Both endometrial hyperplasia (EH) and malignancy (EM) are entities whose diagnosis requires anatomopathological examination. Hyperplasia is defined as an excessive growth of the endometrium with an increased gland to stroma ratio and an irregular glands distribution (23, 24). Since 2014, the World Health Organization (WHO) proposed a new classification of EH which was accepted by the International Society of Gynecological Pathologists, and which divided hyperplasia into two groups: benign hyperplasia and atypical hyperplasia/endometrial intraepithelial neoplasia (EIN) (25). The latter is characterized by the presence of cytological atypia in proliferating overcrowded, sometimes back-to-back glands. These changes are also present in endometrial carcinoma (EC) thus making the differential diagnosis of this malignancy in its lowest grade very challenging to distinguish from the most severe hyperplasias, to such a point that the gold standard for validation of the diagnosis of adenocarcinoma in histopathology is the presence of myometrial invasion by the hyperplastic atypical cells in hysterectomy specimen or deep biopsy (23, 24).

From a diagnostic perspective, the most frequently encountered symptom is AUB in both EH and EM. The International Endometrial Tumor Analysis (IETA) did set a consensus opinion regarding the pertinent sonographic criteria allowing the differential diagnosis between Ep, EH and EM (22) (fig 14). Still, the definitive diagnosis entirely belongs to histopathology.

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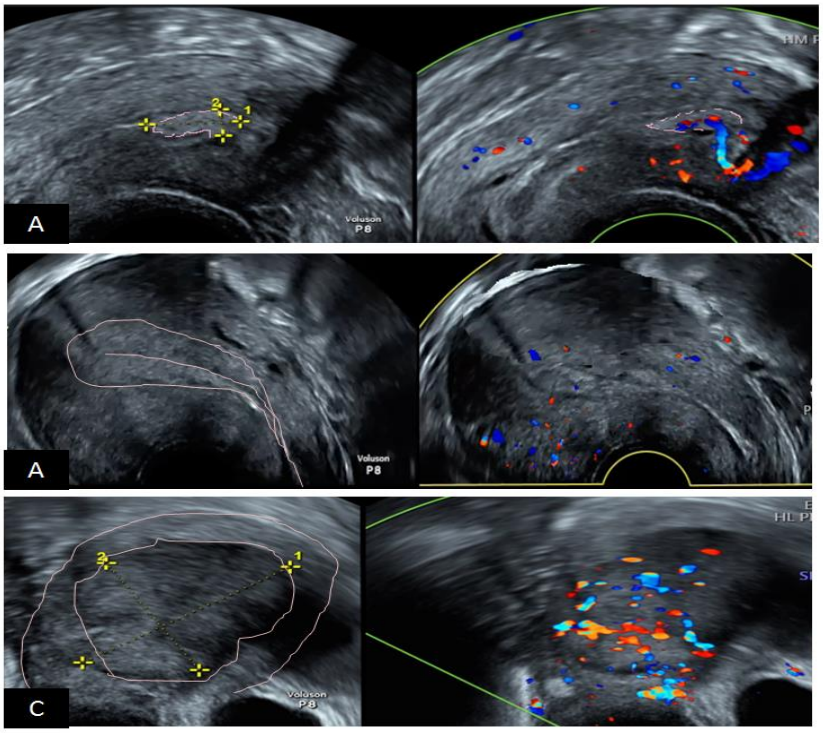

Figure 14. The International Endometrial Tumor Analysis (IETA) consensus opinion regarding the differential diagnosis between EP, EH and EM. A: endometrial polyp hyperechoic with a unique vascular pedicle; B: endometrial hyperplasia with moderate vascularization at Doppler; C: endometrial malignancy, thick image with intense hypervascularization at Doppler. Images by A. Drizi

In terms of diagnostic hysteroscopy, although there is to date no universal and reproducible morphological hysteroscopic definition of EH (26, 27), it is accepted that the condition appears as a diffuse or focal hypertrophy of the mucosa, displaying different patterns (fig 15). Depending on the severity of the thickening, the hyperplastic endometrium will adjust to the cavity's volume by forming more or less big foldings mimicking endometrial polyps yet without a unique vascular pedicle but moderate vascularization. However, if the thickening is uniformly diffuse without any polypoid reinforcements, hysteroscopic diagnosis might be confusing whereas ultrasound allows accurate measurement of the mucosa's thickness (fig 16). In these cases, paying attention to the subtle changes come in handy such as an irregular paler surface with edema, irregular glands distribution and increased micro vascularization.

The main differential diagnosis of EH without atypia is the late secretory phase and the dysfunctional inflammatory endometrium (3, 5).

Atypical EH, also termed EIN, and EC however are likely to display similar patterns both hysteroscopically and histopathological (28).

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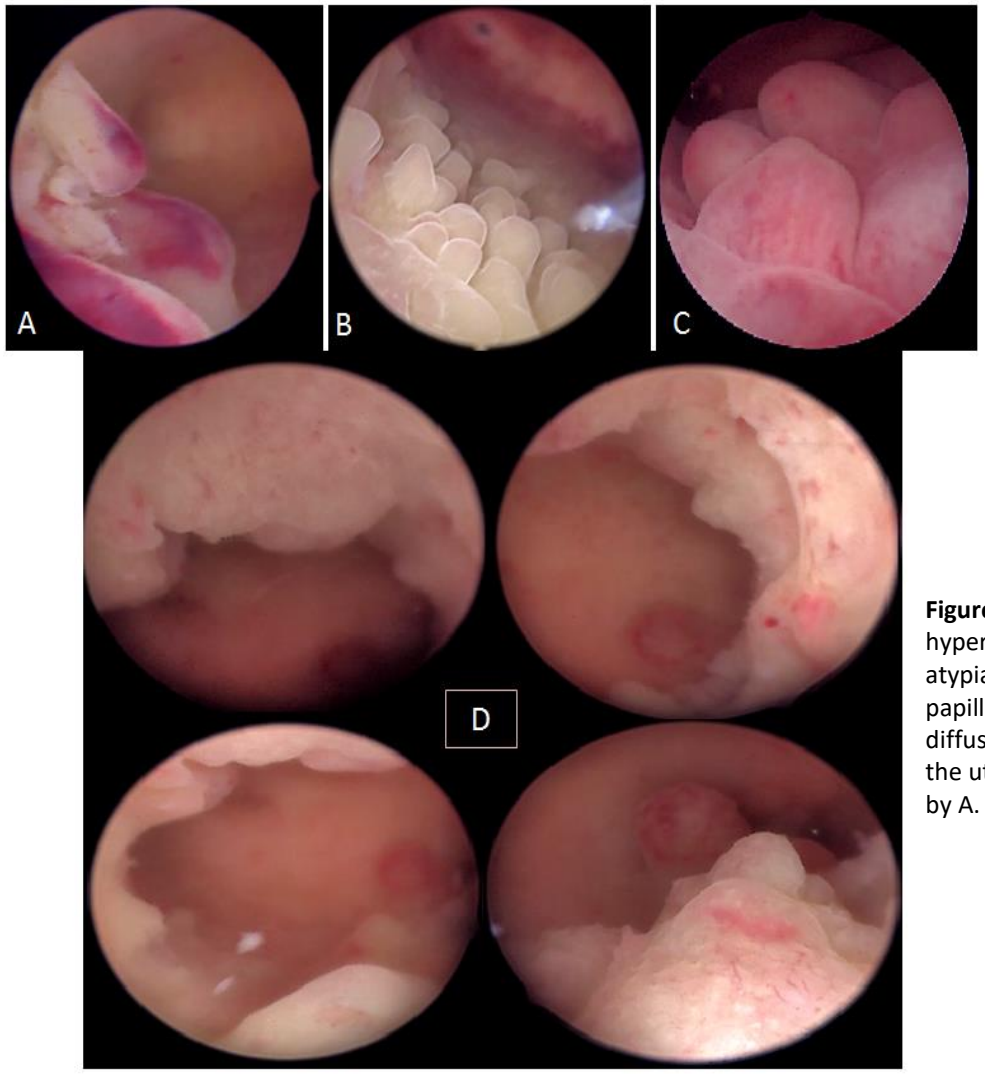

Figure 15. Endometrial hyperplasia without atypia. A: focal; B: papillary; C: polypoid; D: diffuse to the 4 walls of the uterine cavity. Images by A. Drizi**.**

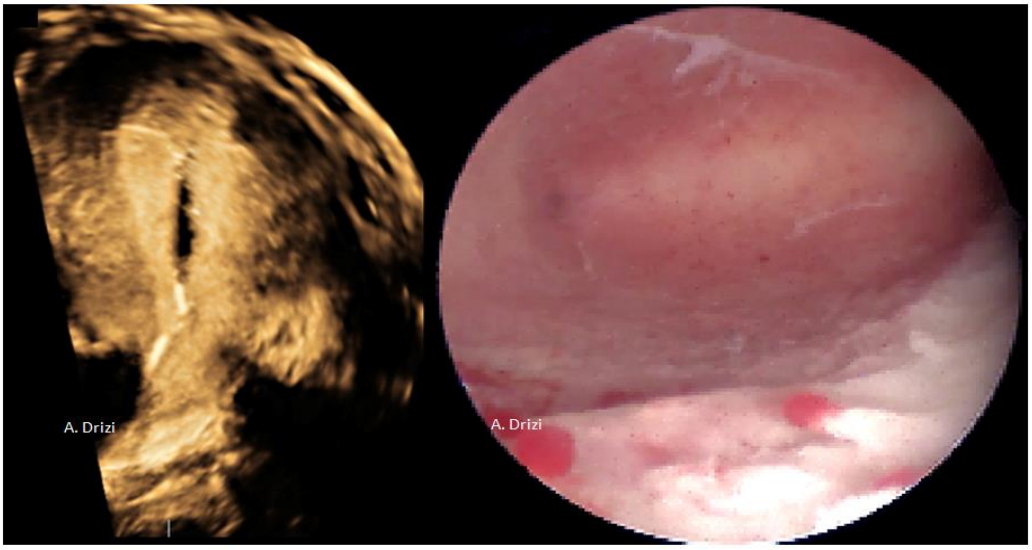

Figure 16. Uniformly diffuse endometrial hyperplasia without atypia. The major role of ultrasound and of the subtle irregularities of the endometrial surface at hysteroscopy.

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EM received higher attention from authors and different classifications have been proposed by different researchers to improve the hysteroscopic identification of the suspicious lesions to be visually biopsied. The neoplastic processes are categorized by their morphological external appearance. The terminology proposed by these classifications describe tumors as nodular (bulging), polypoid (thin pedicles), papillary (numerous dendritic projections), glomerular (polypoid with papillary-like component containing atypical neo-vessels covered by a thin layer of endometrial tissue) and cerebroid (nodular or polypoid with abnormal surface vessels) (29) (fig 17). Other terms were proposed by other authors such as ulcerated (endophytic) patterns and cotton-candy like (presence of necrosis) (29).

However, regardless of the terminology used in these different classifications, all seem to agree on the same morphologic criteria suggestive of atypical EH/EM and which are vascular, glandular and epithelial.

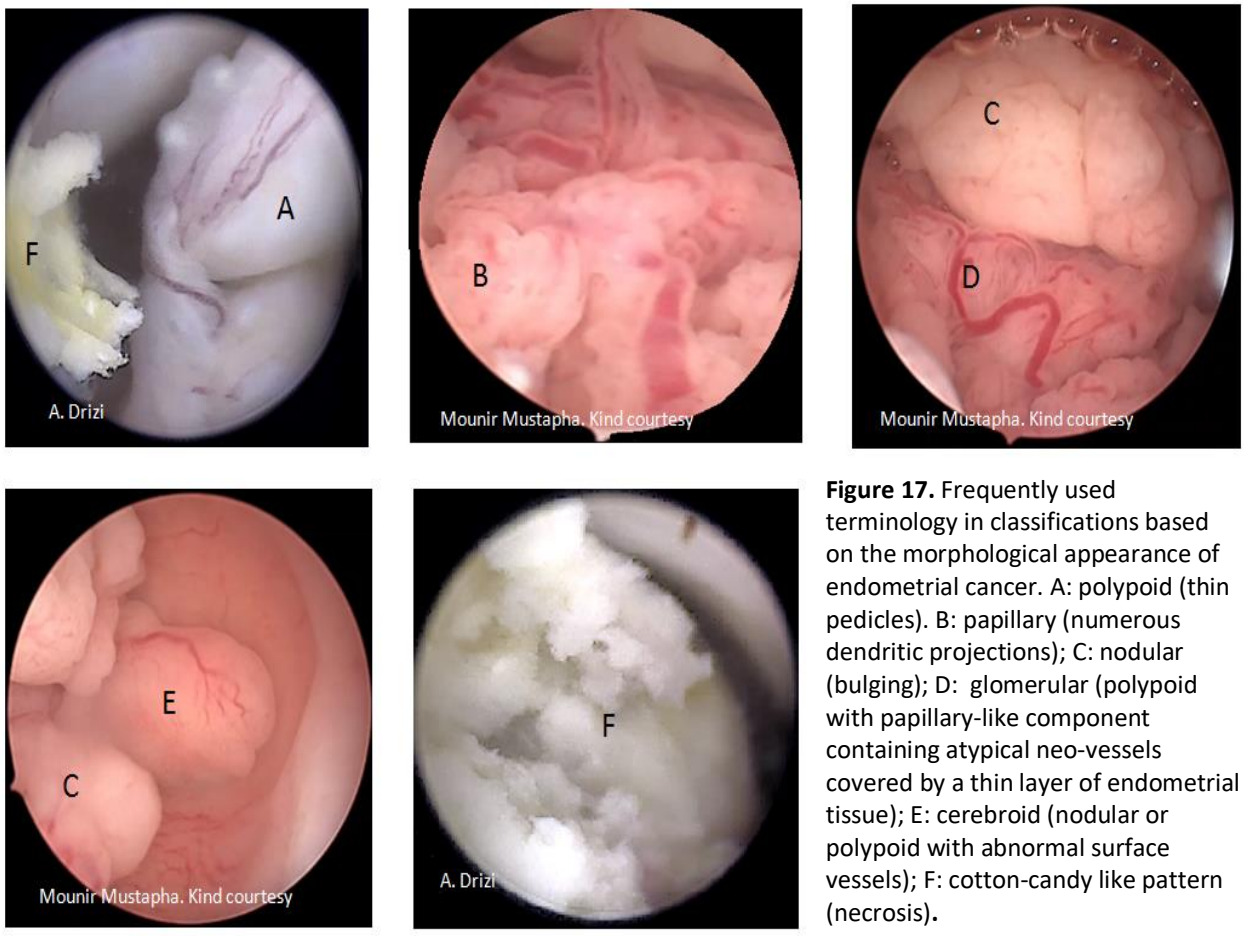

Figure 17. Frequently used terminology in classifications based on the morphological appearance of endometrial cancer. A: polypoid (thin pedicles). B: papillary (numerous dendritic projections); C: nodular (bulging); D: glomerular (polypoid with papillary-like component containing atypical neo-vessels covered by a thin layer of endometrial tissue); E: cerebroid (nodular or polypoid with abnormal surface vessels); F: cotton-candy like pattern (necrosis).

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Consequently and educationally speaking, it could be more interesting to focus on the analytic details of the tissue and vessels instead of the various classifications themselves. Those criteria indicate the site where the biopsy has to be performed, as all researchers confirmed their suspiciousness and use them to assess the risk in the above mentioned classifications. In addition to the lesion's thickness (10 mm or greater) and its extension to the cervix, the morphologic epithelial criteria to be particularly careful about are illustrated in fig 18 and consist of an irregular surface (polypoid, endophytic or exophytic projections), heterogeneous colors (whitish-grayish without vessels on the surface: indicators of glandular back-to-back overcrowding; yellowish or whitish cotton-candy aspect as indicator of necrosis). The more the tissue is friable and hemorrhagic at hysteroscopic manipulation, the more suspicious (fig 18). And just as importantly, the characteristic suspicious vascular patterns present with irregular diameter, irregular ramifications, brutal interruptions and serpiginous trajectory forming loops at places (29,30) (fig 19).

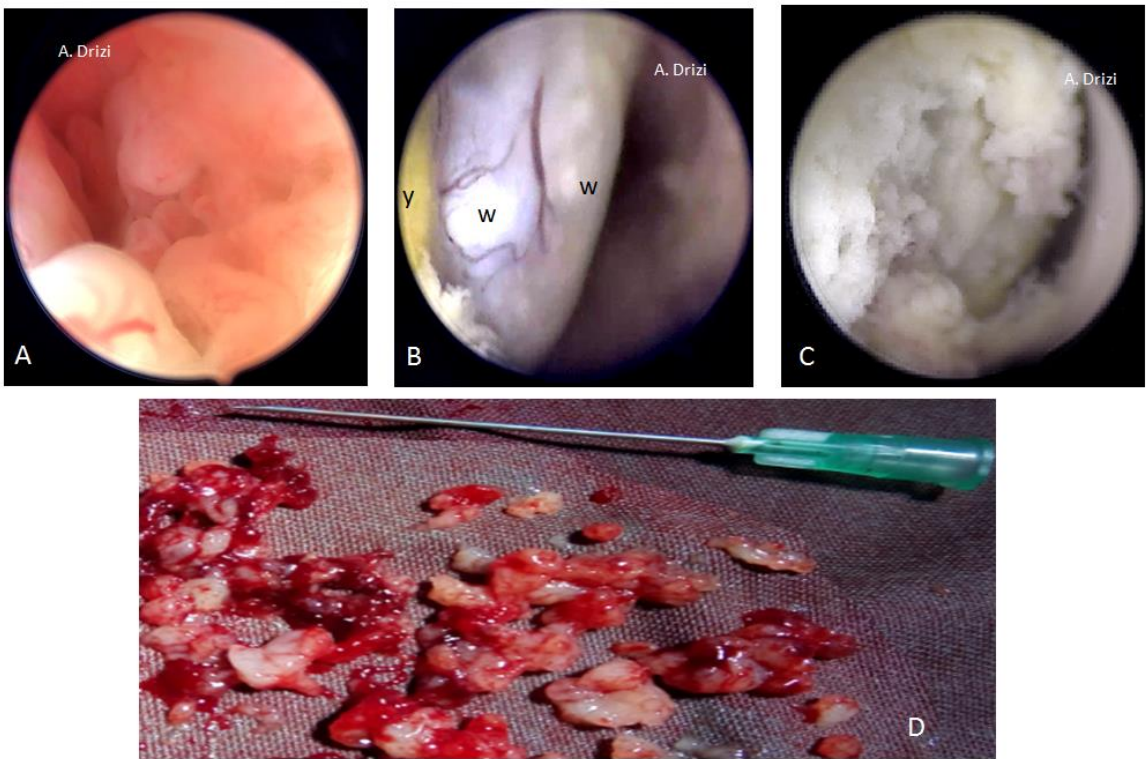

Figure 18. The morphological epithelial patterns suggestive of atypical EH/EM requiring attention and sampling. A: irregular surface (polypoid, endophytic or exophytic projections); B: heterogeneous colors: whitish-grayish surface without vessels (w) (back to back glands); yellowish (y) (necrosis); C: yellowish and whitish cotton-candy aspect (necrosis); D: friable hemorrhagic tissue both at hysteroscopic manipulation and at macroscopy.

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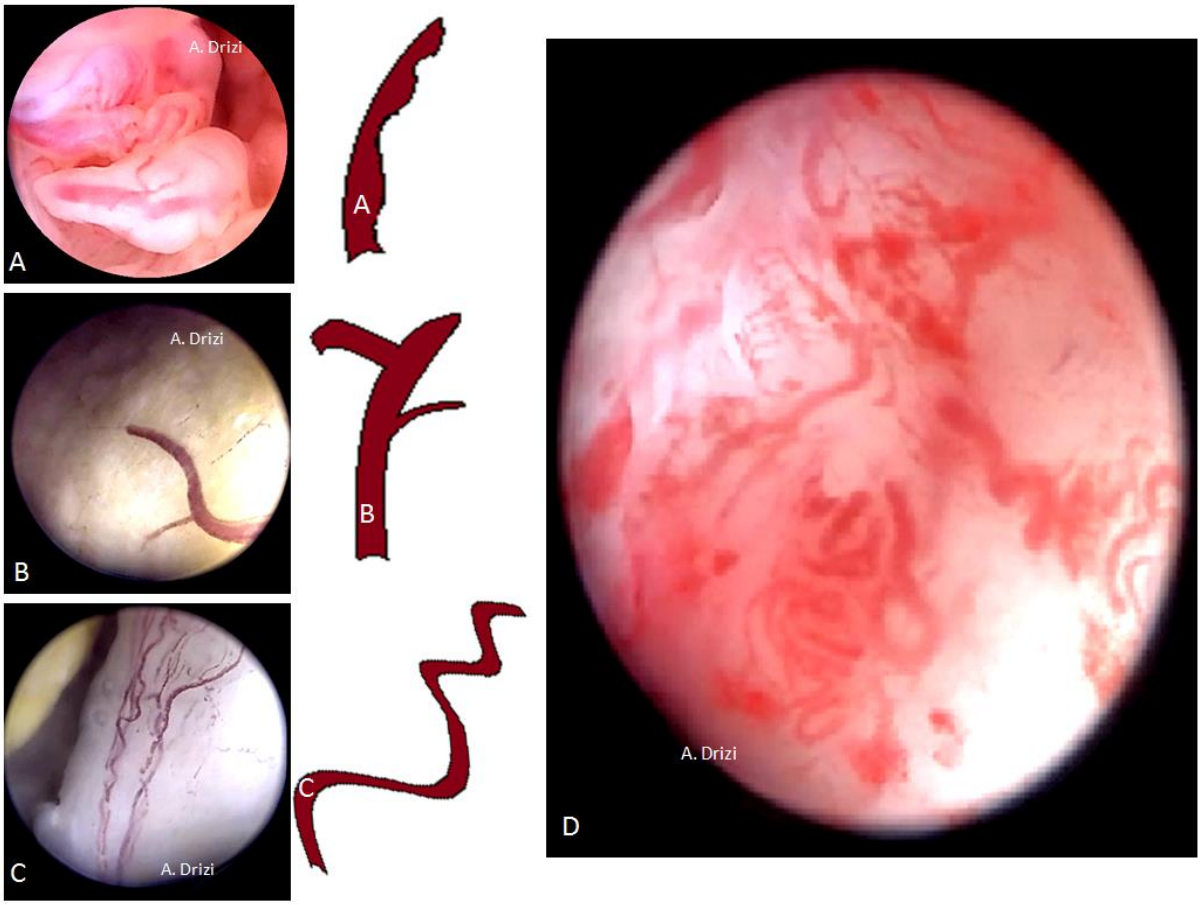

Figure 19. The morphological vascular patterns suggestive of atypical EH/EM requiring attention and sampling.
A: irregular diameter; B: irregular ramifications and brutal interruptions; C: serpiginous trajectory forming loops at places; D: different atypical vascular patterns at microhysteroscopy. Images by A. Drizi

General principles of sampling.

The techniques of sampling are addressed in a separate article of this special edition. Nevertheless, the general principles related to tissue processing and examination by pathologists will be highlighted in order to grow awareness on the necessity of good practice.

Because endometrial pathology is more commonly focal than diffuse (7), it is necessary to perform the sampling within the area displaying anomalies. The amount of tissue has to be sufficient and oriented so as to optimize the chances of a correct diagnosis by pathologists who need to receive proper information about all the cases.

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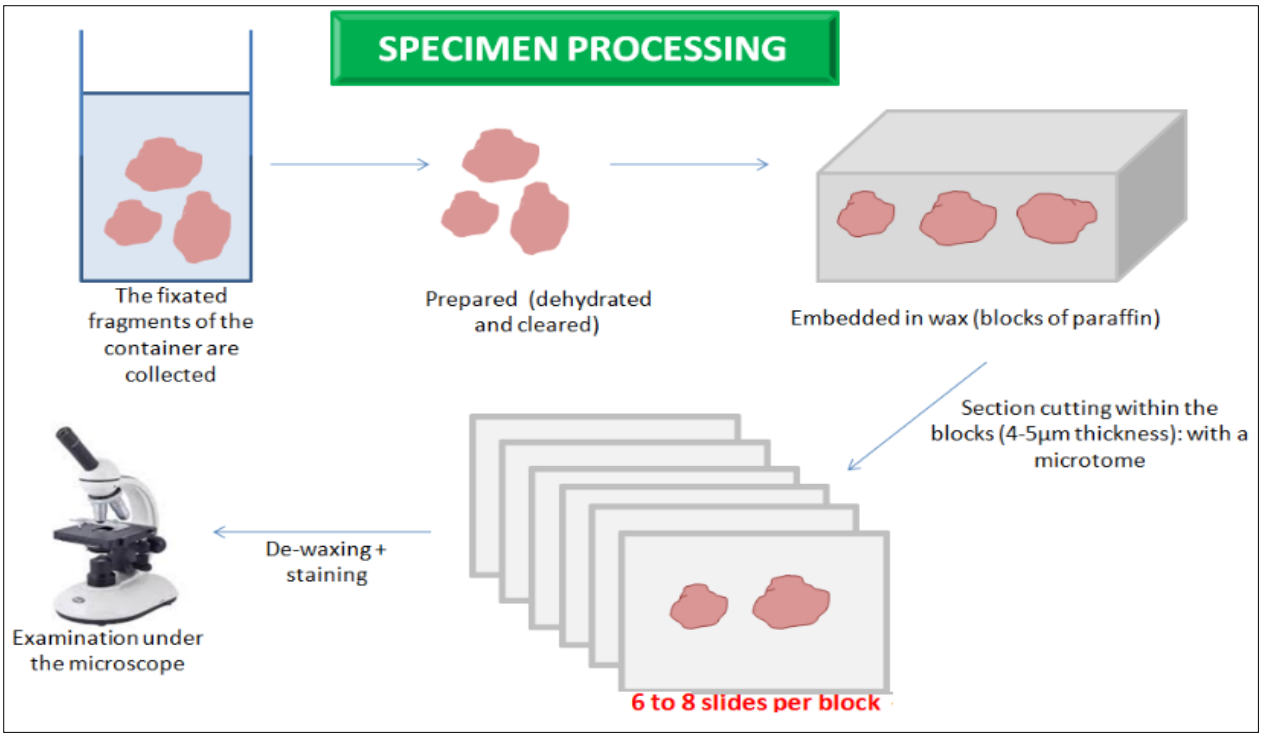

Figure 20. Specimen processing in histopathology. The main steps.

To ensure sufficient amount of tissue, different instruments can be used such as graspers, scissors, the loop of a min resectoscope or a tissue removal system. Because of the limited number of cuts pathologists universally perform (fig 20), it is always best to label and send in a separate container whatever lesion displaying suspicious or different aspects from the other lesions. To avoid further artifacts, the sample needs to be handled with gentleness, without compression –as it could create a false back to back distribution of glands– and always placed in a correct conservative milieu made of 15 volume equivalents of 10 % formalin per volume of tissue (31).

The descriptive report

After hysteroscopy, a document reporting all the procedure's findings with the backing iconography has to be delivered to the patient. In table 2 is proposed a summary descriptive report addressing in a systematic way each step of the procedure.

DOI: 10.36205/trocar1.2023006

Name of the hysteroscopist **Date of the procedure**

Name of the patient
Date of birth
Obstetrical history
Medical history

Indication and context of hysteroscopy (example: abnormal uterine bleeding in subfertility context)
Day and length of the menstrual cycle Vs menopausal statue.

With or without anesthesia (type of anesthesia if performed).
Lithotomy position
Specify the used equipment (example: 5mm continuous flow office hysteroscope, 2.9mm scope of 30° angle)
Describe:

- The vagina
- Ectocervix (ectropion, stenosis, endometriosis etc.)
- Endocervical canal (orientation, mucosa, mucous, lesions…)
- Uterine isthmus whenever possible: better examined during the retrieval of the scope (orientation, length, niche, lesions).
- Uterine cavity: shape, size and tubal ostia.
- Eventual intrauterine pathology: description of type, dimension and location
- Endometrium: in comparison with the phase of the menstrual cycle/menopause. Thickness, glands, color, vessels, inflammatory patterns, etc
- Note the presence or absence of hysteroscopic signs for atypia/malignancy.
- Note whatever incident or unusual finding.

Describing the sampling technique/site/containers and/or the operative procedure performed (used equipment; fluid deficit)
Pain level (if no anesthesia).
Iconography

Signature

Table 2: proposed systematic descriptive report.

Conclusion

In the era of "see and treat", performing a hysteroscopy with a diagnostic sheath just to see and leave has become derisory. An operative sheath with a working channel containing an instrument (graspers or scissors) is the minimum for entry in diagnostic hysteroscopy so that a targeted biopsy and/or removal of pathology are done within the same diagnostic session whenever possible.

The prerequisite for the practice of diagnostic hysteroscopy is growing knowledge of the normal and pathological endometria so as to improve the quality of diagnosis, also by providing good quality visual sampling. The frequently focal character of most benign,

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premalignant and neoplastic endometrial lesions highlights the importance of a proper sampling within the lesion site, which blind procedures are more likely to miss.

Atlas-like overviews are interesting to visualize in order to memorize the problematic patterns requiring more attention.

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Structure and Appearance of Endometrial Blood Vessels at Hysteroscopy

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The author declares no conflict of interest.

Abstract

By using the hysteroscope in contact mode to observe the endometrial vasculature, it became possible to correlate the appearance of the endometrial vasculature to the different phases of the human menstrual cycle This allows to date the endometrium and to compare the normal appearance of the endometrial vasculature with the endometrial vasculature in cases of pathology originating from the endometrium leading to physical complaints of the patients.

Key words:

Endometrium; hysteroscopy; vessels; visual appearance; glandular structure; histopathology; biopsy.

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Introduction

Endometrial blood vessels play an important role in the various physiological phases of the menstrual cycle. The presence of the specific vessels and their structure allows for identification of the different phases of the menstrual cycle corresponding with the histopathological dating (1-2). On the other hand, in different pathologies the appearance of the endometrial vessels is a primordial indicator like in Abnormal Uterine Bleeding (AUB), endometrial polyps, fibroids, polyps, adenomyosis, hyperplasia, endometrial related infertility and pill endometrium. Endometrial vessel angiogenesis allows to recognize the difference between vessel concentration and appearance in the basal and functional layers of the endometrium, congestion and dilatation as visualized by hysteroscopic examination (3). The recent scientific evidence that the vertical endometrial glands in the functional layer of the endometrium originate from a bed of horizontal glands in the basal layer of the same endometrium leads to the better understanding of the endometrial vessels both in the basal and the functional layer (fig 1). The vessels are feeding the glands by a network of side arborization from the main vertical vessel. The study proves that dating of the endometrium by observing the structure of the vessels is feasible and correlates with the histopathology of the biopsies.

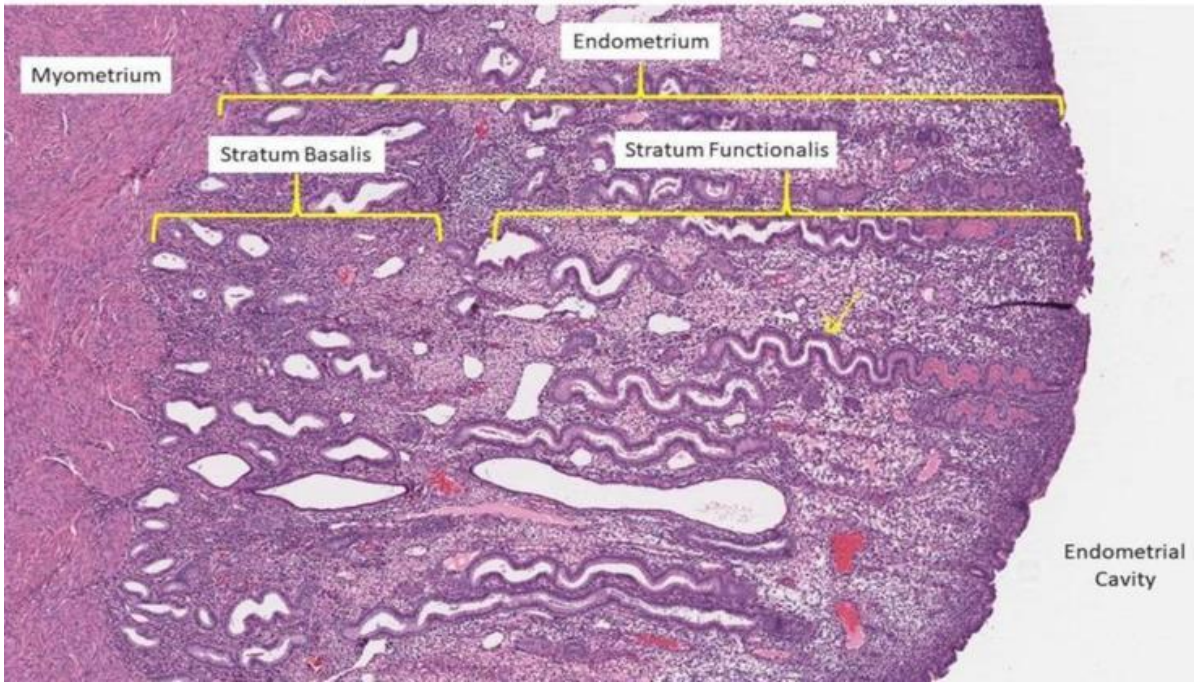

Figure 1. Different layers: from myometrium over endometrium showing vessels and endometrial glands. Stratum Basalis remains during menstruation whilst the Stratum Functionalis is shed.

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Material Method:

To identify the hysteroscopic appearance of vessels in the normal endometrium, the original study was performed at 200 consecutive hysteroscopies in consenting, healthy, patients in their fertile age, with normal menstrual cycles as evidenced by hormonal essays (estrogen, progesterone, FSH and LH) and recorded cycle days. In the final study 173 patients have been retained as 27 patients did stop during the study because complaints of too intense discomfort at hysteroscopy or irregular cycles. The patients presented with normal cycles and no complaints.

All hysteroscopies of the original study (1984-85) have been performed under CO_2 dilatation of the uterine cavity at a pressure of 60 mm Hg (Richard Wolf GmbH Knittlingen Germany 2121 CO_2 Metromat®). CO_2 distention was used because at the time of the study this was the only existing method of distention available to perform hysteroscopy (1-2).

The hysteroscope used was a Hamou I Micro 30° for oblique, 6 mm diameter rounded hysteroscope (Karl Storz SE & Co KG Tuttlingen Germany) with magnification from 1:1 to 150:1 (1-2). For the study, an enlargement 1:60 has been used. Without prior dilatation, so as not to interfere with the endometrium, the hysteroscope was introduced in the uterine cavity and brought into contact with the endometrial surface on the anterior wall near the fundal area and the CO_2 inflow was stopped. The image was focused and recorded (Olympus OM 2 camera, zoom 70-140 mm).

The performing hysteroscopist was blinded not knowing the exact phase of the cycle of the specific patient. Based on SRM Reynolds diagrammatic representation of the endometrial glands and arterioles, the arterioles throughout the menstrual cycle did allow a division of the endometrium into five periods by the visual impressions of the vessels (4) (Tab 1) (fig2). Initially the vascular pattern could be made out and the correspondence with the pathology of the original study is listed in Tab 2. Later fluid distention has been used and due to the fact that the endometrium with fluid distention is less compressed against the uterine walls dating of the endometrium by hysteroscope did become more accurate reaching an accuracy of around 96 % correspondence with pathology in expert hands. At the time of the study, historically, there was no need for Ethical Committees approval of the study.

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			Day of Cycle
1	**Early Proliferative Phase**	**EPP**	**3-8/28**
2	**Late Proliferative Phase**	**LPP**	**9-13/28**
	Ovulation Phase		***14-16/28***
3	**Early Secretory Phase**	**ESP**	**17-22/28**
4	**Late Secretory Phase**	**LSP**	**23-25/28**
5	**Premenstrual – Menstrual Phase**	**PMMP**	**26-28/28**

Table 1. Hysteroscopic dating of the endometrium according to the days of the cycle.

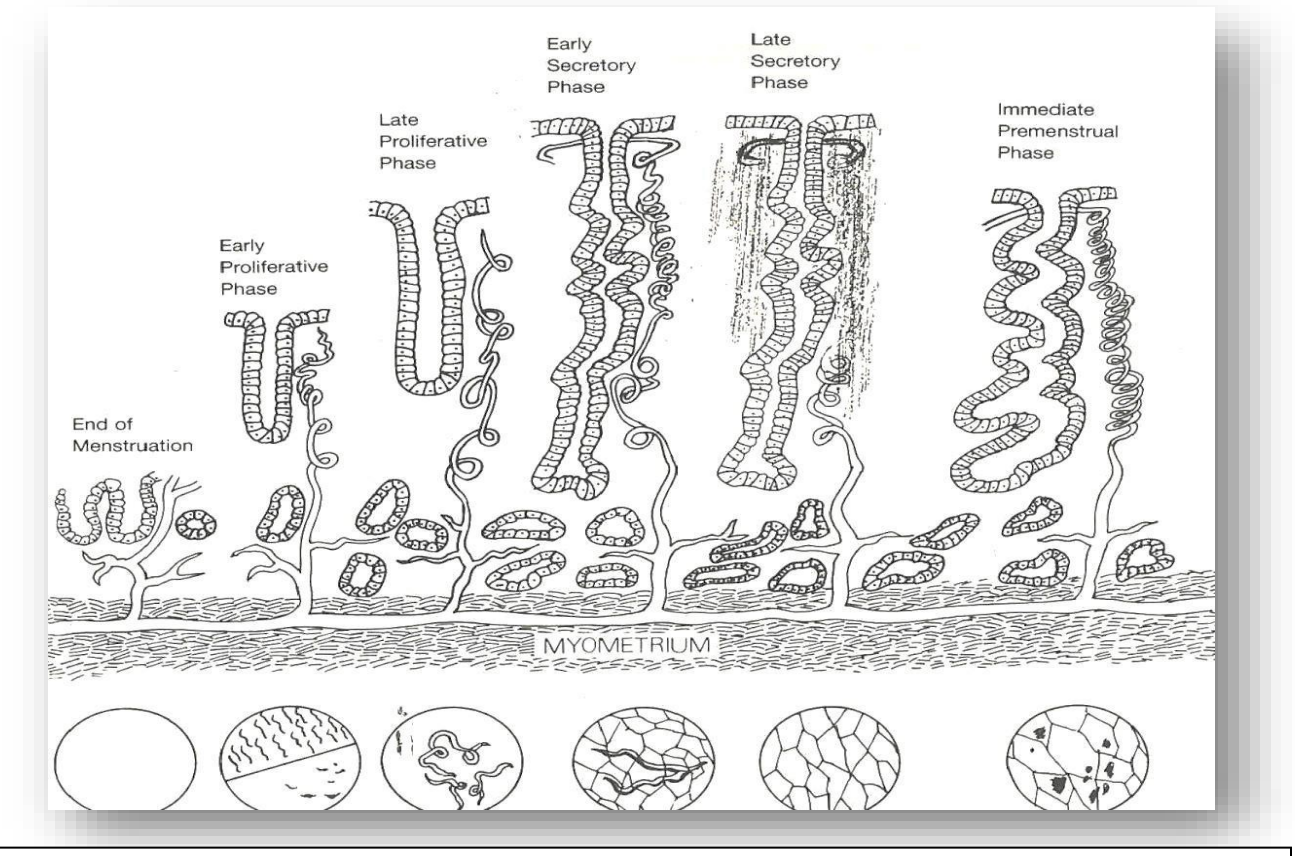

Figure 2. SRM Reynolds drawing of the endometrial growth to maximal height and decreasing height prior to menstruation with adaptation (BvH 1987) on densification of the interglandular tissues and schematic corresponding representation of the hysteroscopic view in lower part.

DOI: 10.36205/trocar1.2023007

	Number of cases		**Histopathologic Dating**[1]	
			n	**%**
EPP	25	**EPP**	**18**	**72**
		LPP	1	4
		ESP	3	12
		Hypotrophy	3	12
LPP	23	**LPP**	**16**	**69,7**
		EPP	1	4,3
		ESP	2	8,7
		LSP	3	13,0
		Hypotrophy	1	4,3
ESP	32	**ESP**	**26**	**81,3**
		LPP	4	12,5
		EPP	2	6,2
LSP	13	**LSP**	**7**	**53,8**
		ESP	4	30,8
		LPP	2	15,4
PM-MP	10	**PM-MP**	7	**70**
		ESP	2	20
		Hyperplasia	1	10
[1] Number and percent frequency distribution				

Table 2. The numbers of the dating by hysteroscopy and by histopathology. The dating as given by the blinded hysteroscopists and the respective corresponding histopathology diagnoses and percentages are listed.

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Results

According to the visual impression through the hysteroscope correlated with the anamnestic, hormonal and pathology data, the human menstrual cycle could be divided in five stages:

1. Early proliferative phase (EPP) day 3-8/28.

This stage is divided in two sub stage the very early-stage day 1-3/28 and the later phase day 4-8.

1. a) In the early stages blood can still be seen and there is a white reflection of the upper part of the myometrium though the basal endometrium – the endometrium that is not shedded during the menstruation – and the basal arterioles are visible running parallel with the myometrium and parallel to each other (Fig 3).

1. b) In the later EPP (day 4-8) the endometrium gains a pinkish colour due to the increase in height now it is the radial arterioles that grow vertically in the functional layer of the endometrium that are seen as comma like structures pointing upwards (Fig 4).

Figure 3. Early Proliferative Phase (CD 01-02). There is still blood in the cavity. The light is reflected on the basal layer of the endometrium. Basal arteries are seen running parallel with each other in the horizontal plane. (CO_2 distention 60 mm Hg).

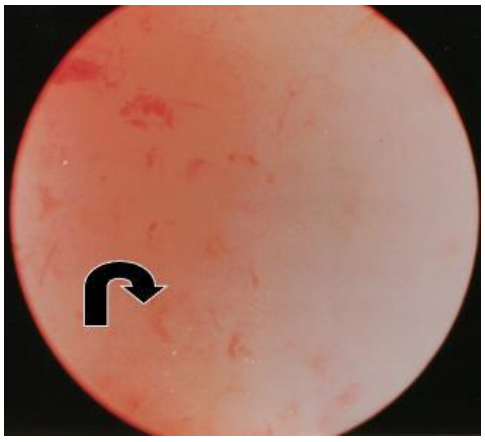

Figure 4. In the later phase of the Early Proliferative Phase (CD 3-8) the arcuate arteries are growing to the lumen of the uterine cavity – vertical as opposed to the basal arteries. These arterioles are seen as pointing upwards. (CO_2 distention 60 mm HG)

DOI: 10.36205/trocar1.2023007

2. Late proliferative phase (LPP) day 9 – 13/28.

This is the stage where the coiled arteries grow off the radial arteries to grow alongside the endometrial glands to feed the latter. The anatomical aspect of these coiled arterioles – called spiral arteries in the original articles – can only be seen by pressing the hysteroscope into the growing functional layer of the endometrium. The overall colour aspect of the endometrium remains pale pinkish due to the extremely rapid growth in height of the functional layer of the endometrium (Fig 5).

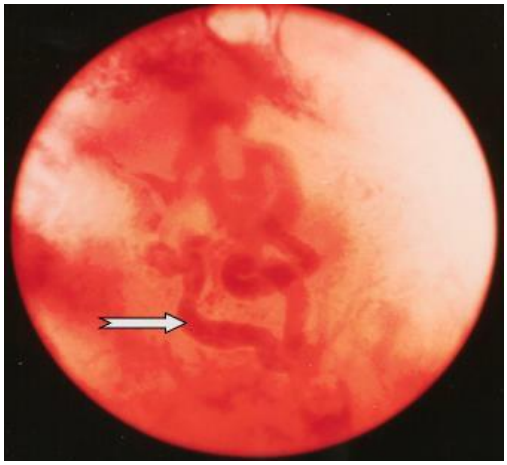

Figure 5. Late Proliferative Phase (CD 09-13). The main features are the coiled arterioles developing as the continuation of the radial arterioles. Only seen when penetrating the functional endometrium with the hysteroscope. (CO_2 distention 60 mm HG)

3. Early Secretory phase (ESP) day 17-22/28.

In this phase the endometrium is at its maximum height and due to the physiological oedema of the interglandular tissue it is transparent. Here the scope is able to visually interpret arterioles some 6 µ under the surface. The end part of the coiled arterioles can be seen whereas very small arterioles surrounding the glandular openings cross over these end parts. Moving the tip of the scope gently on the surface makes that these very small arterioles shift with the scope and the end parts of the coiled arteries remain in place giving rise to a two layered endometrium. The overall colour impression of the endometrium is very pale pink (Fig 6).

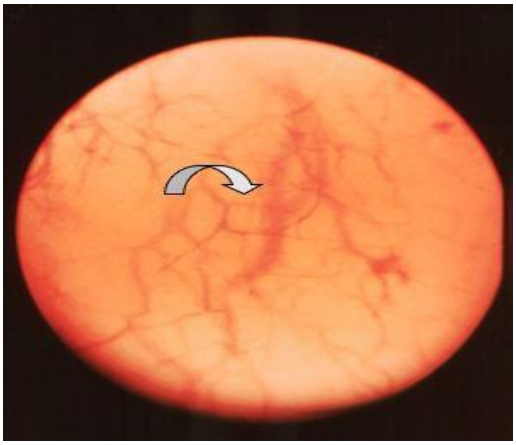

Figure 6. Early Secretory Phase (CD 17-22). The two layered endometrium. The final part of the coiled arteriole is seen and the fine maze of the arterioles surrounding the endometrial gland openings are seen running over the coiled arterioles. (CO_2 distention 60 mm HG)

4. Late Secretory phase (LSP) day 23-25/28.

DOI: 10.36205/trocar1.2023007

The densification of the intra glandular tissues of the endometrium, in this stage of the cycle, makes it impossible to visualize the coiled arterioles. The only vascular structures visible are the small arterioles around the endometrial glandular openings. The colour impression now turns to ivory (Fig 7).

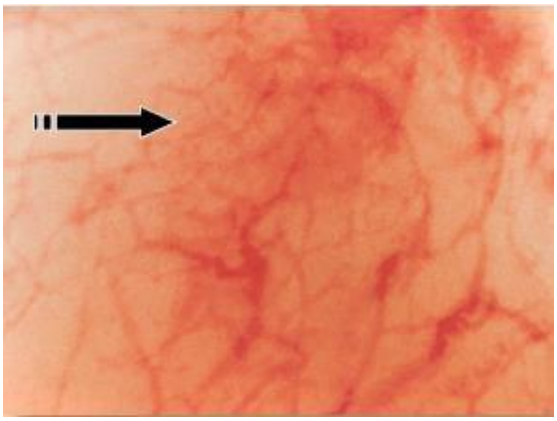

Figure 7. Late Secretory Phase (CD 23-25) Due to the densification of the interglandular tissues the final part of the coiled arteries is no longer visible. The arterioles surrounding the glandular openings are prominent in view. The colour becomes more ivory. (CO_2 distention 60 mm HG)

5. Premenstrual – Menstrual phase (PM-MP) day 26-28/28

In this phase the contact hysteroscopy is no longer needed. On the surface of an ivory-colored endometrium red dots are observed (Fig 8). These do correspond by sub- epithelial bleedings. Due to the decrease in height of the endometrium the coiled arteries start to leak to form dissecting hematomas. These will then cause the shedding of the functional layer of the endometrium starting at the cornu in spiral like fashion (Fig 9).

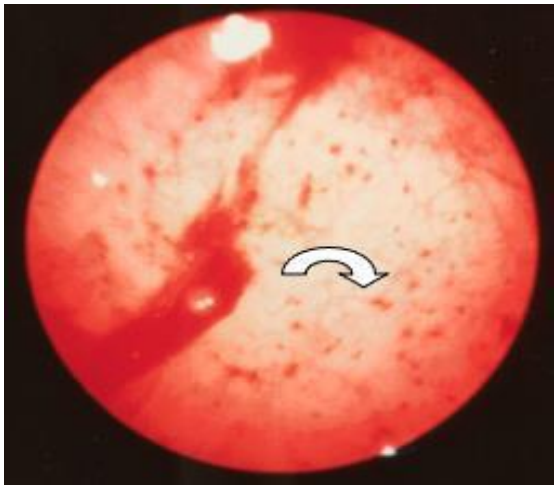

Figure 8. Premenstrual and Menstrual Phase (CD 26-28). Due to the shrinkage of the interglandular tissues the coiled arteries begin to leak and form dissecting hematomas inducing the shedding of the functional layer of the endometrium. The blood collections seen are not in the glandular openings but in the interglandular tissues. (CO_2 distention 60 mm HG)

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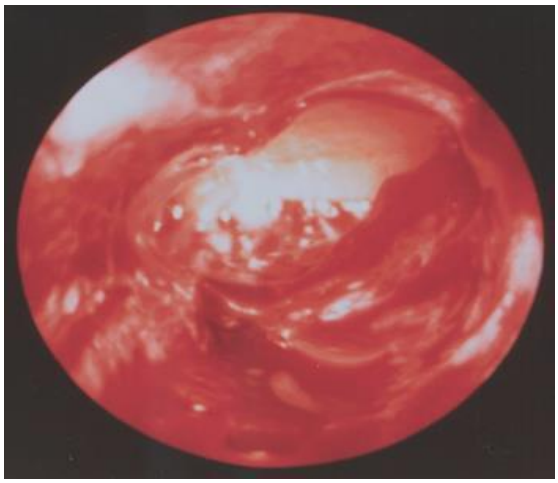

Figure 9. Menstruation. The fundus is already denudated. Remark the patches of functional endometrium still present whilst the endometrium is expulsed in a spiral fashion starting at the cornual parts of the uterine cavity. (CO_2 distention 100 mm HG)

Discussion:

First of all, it has to be noted that pinpointing the ovulation phase by the visual impressions of the vessels trough the hysteroscope, the original scope of the study, averred to be an illusion due to the fact that hormonal changes do occur first and anatomical changes do follow the latter (5). This study did lead to the division of the cycle in five periods, phases, according to the visual appearance of the arterioles as described in the results, in correlation with the anamnestic data and the pathologic results obtained by direct biopsies through the hysteroscope (1-2). These results have been obtained by CO_2 gas distention of the uterine cavity. This gas does induce hyperemia causing the arterioles to be better visible. In the later observations distention fluid has been used. This method of distention allows for the endometrium to "hang" into the uterine cavity allowing for a better detailed observation of the vessels and therefore for a more accurate interpretation (6). With the normal vasculature in mind, focus can be turned on interpreting the visual features of the arterioles of the endometrium in patients with endometrial abnormalities. Histopathology does describe changing in vessel concentration with a significant higher concentration in complex hyperplasia and pill endometrium whilst congestion and dilatation is significantly higher in patients with AUB (3) (Fig 10). These changes can be observed at hysteroscopy even without contact mode. The recent findings concerning the microanatomy of the endometrial glands does strengthen the results of the first studies as the "vertical" glands have a feeding vessel with lots of arborizations, the described coiled arterioles (7 - 8) (Fig 11).

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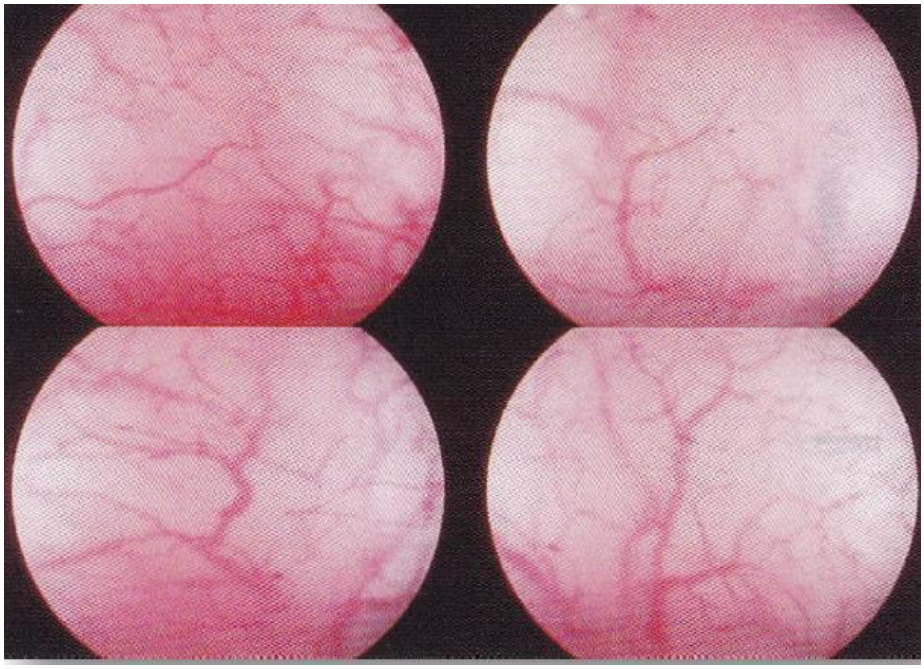

Figure 10. Pill endometrium. The very pink colour is due to an increased numeric presence of vessels, in a significantly higher concentration than in the normal.

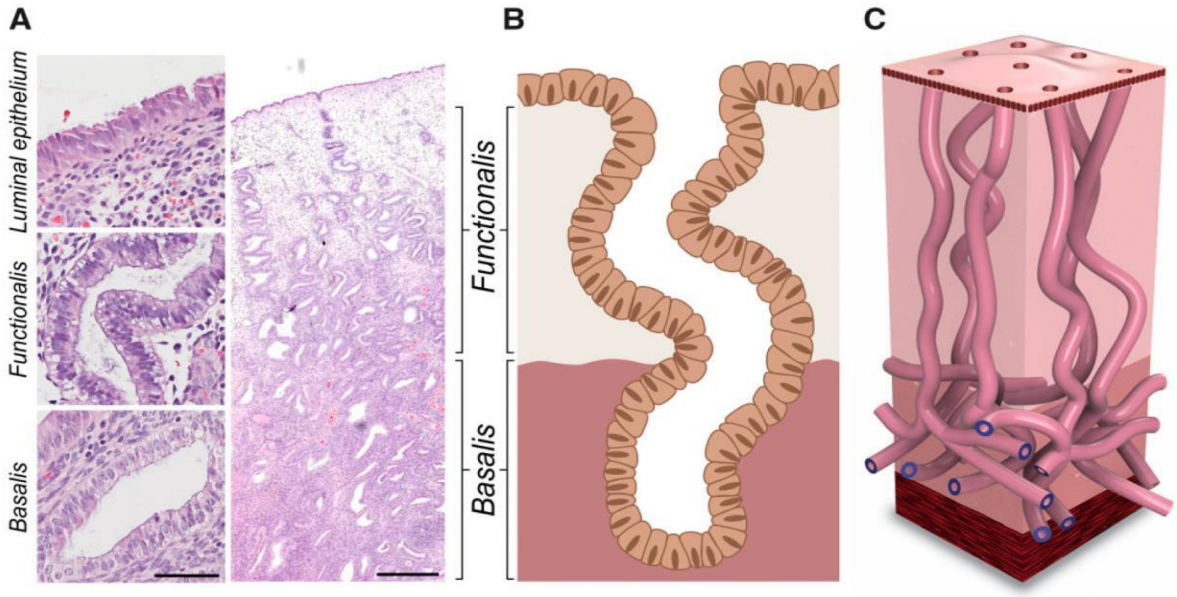

Figure 11. Architecture of human endometrial glands: past and present: (A) Hematoxylin and eosin-stained human endometrial section at x400 and x 20 magnification (scale bars= 50 and 500 µm, respectively). (B) 2 D scheme of the pre--2020 consensus view of endometrial glandular architecture, with functional glands running a vertical course to the basalis gland and terminating in blind pouches. (C) 3D scheme of the novel endometrial gland arrangement based on recent findings, with basalis glands exhibiting a branching, mycelium like configuration running perpendicular to functionalis glands (Tempest N, Hill C J, Maclaen A, Marston K, Powell SG, Al-Lamee H, Hapangama D. Novel microarchitecture of human endometrial glands: implications in endometrial regeneration and pathologies. Hum Reprod Update 2021;28(2):153-171)

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There is also the need to harmonize the denomination of arterioles by both gynaecologists and pathologists in the different phases of the cycle.

Conclusion:

Observing the endometrial arterioles during routine hysteroscopy does give valuable information concerning the phase of the cycle and even on possible symptoms as perceived by the patient.

However, as the studies on visualization of the arterioles in the endometrium have been performed in the period of CO_2 distention, there is need for large clinical observational studies with liquid distention media.

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Diagnostic hysteroscopy for submucous myomas

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The authors declare no conflict of interest.

Abstract

Uterine myomas are very commonly found in women of reproductive age. Diagnostic and simultaneous operative hysteroscopy is the cornerstone of treatment of submucous myomas. This non-systematic review aims to outline the role of diagnostic hysteroscopy in patients with submucous myomas, and the surgical assessment of these myomas as regards technique of surgery and level of difficulty before initiating myoma resection.

Key words:

Hysteroscopy; fibroids; myomas; polyps.

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Introduction:

Uterine myomas are the most common benign pelvic tumours of the female genital tract [1]. Their incidence is approximately 25%–30% of all women in the reproductive age, and can be higher depending on race, family history, and genetics. Submucosal fibroids have a consistent association with heavy menstrual bleeding and infertility [2].

Hysteroscopy is the most commonly used tool for diagnosis and simultaneous treatment of patients suffering from abnormal uterine bleeding, recurrent abortions and infertility. Among many other pathologies that are responsible for these symptoms, uterine myomas are one of the most commonly found. Diagnostic hysteroscopy plays an important role in decision making regarding the treatment of submucous myomas. Hysteroscopic myomectomy is the first line minimally invasive and conservative surgical treatment. In this non systematic review, we will attempt to present the exact place of hysteroscopy in patients with submucous myomas from an exclusively diagnostic perspective.

The importance of Imaging

Before a surgery can be planned, a thorough assessment of the size, number and location of the fibroids is done. Conventional 2D ultrasound is sufficient to localize and map the fibroids in most cases. A saline infusion sonography delineates the cavity and provides valuable information about the extent of intra cavitary extension in case of submucous myomas. More detailed fibroid mapping using a high resolution 3D ultrasound or MRI may be used in larger or multiple fibroids, or when a diagnostic confusion arises to differentiate a fibroid from focal adenomyosis [3] [fig 1]**.**

Many of the factors involved in assessment and planning of the surgical details are available from the imaging itself, and only need to be confirmed by diagnostic hysteroscopy before operative removal starts. A more detailed account of this is available in the article “Diagnostic hysteroscopy: patient assessment and preparation” in this issue.

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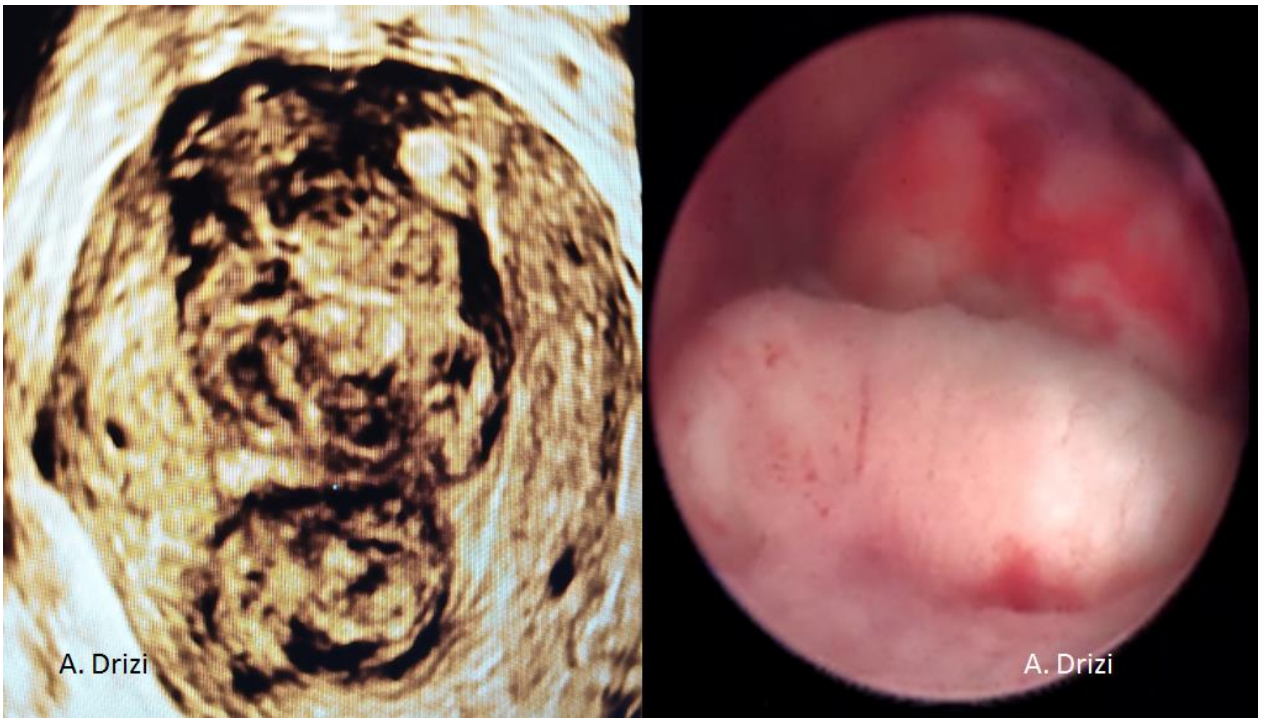

Figure 1. Correlations between 3D ultrasound and diagnostic hysteroscopy. 2 large submucous myomas located in the corpus and in the fundus with different surface vascularization. Images by A. Drizi

Patient preparation

The patient is preferably scheduled for surgery in the early proliferative phase of the menstrual cycle. This ensures that the endometrial lining is at its minimum thickness, and smaller fibroids are not missed during the primary examination because of being buried below the thick endometrial layer.

If the timing of surgery cannot be decided in accordance with the menstrual cycle, or for patients who have irregular cycles, pre operative administration of GnRH analogues helps to thin the endometrial lining **[4].** However, if the diagnostic step through hysteroscopy is necessary, especially in patients with intermenstrual abnormal uterine bleeding, hormonal treatment will represent a diagnostic bias and hence needs to be avoided. In these cases, it is best to schedule hysteroscopy in the early or mid proliferative phase.

The purpose of performing a diagnostic hysteroscopy

The primary purpose of performing a diagnostic hysteroscopy is for assessing the feasibility of the surgery, operative time, assessment of risk and the need for a concomitant diagnostic laparoscopy. It also helps to differentiate a typical submucous myoma from other intra

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cavitary pathologies like a polyp, an adenomyoma/ atypical adenomyoma, and a cerebroid or nodular carcinoma, to name a few [fig 2-6]. A concomitant biopsy can also be performed in an office setting, if the patient is scheduled for an operative procedure under anaesthesia at a later date or if the tumour is enucleated and left inside the cavity for spontaneous expulsion.

Figure 2. Vascular architecture over fibroid. Image by S. Pisat.

Procedure

The patient, under anaesthesia is placed in the lithotomy position, or is comfortably seated in an examination chair specifically designed for an outpatient procedure.

The authors prefer to use a 2.9 mm 30 degree hysteroscope with a bettochi sheath for performing the procedure under or without anaesthesia. A hysteromat with a set pressure of 120 mm Hg is used, at a flow rate of 0.5 to 1 litre per minute. For outpatient procedures, a 1.9 mm telescope, when available, may allow an easier entry into the cavity, particularly in patients with stenosis of the internal os.

Intra operative assessment of the myoma(s)

Typically, a submucous myoma is seen as an inward projection of the uterine wall. More

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intracavitary myomas (FIGO type 0/ type 1) are easily identified as obvious intra cavitary masses projecting from one of the walls or the fundus. Type 2 and 3 fibroids may often be hidden from view due to the overlying endometrial hypertrophy, and hence the importance of performing the procedure in the post – menstrual phase. A typical vascular architecture of fine blood vessels is seen over the surface, visibly different from the endometrium surrounding the mass [fig 2].

It is firstly important to differentiate a submucous myoma from a polyp. A polyp is seen as a fleshy mass that is soft in consistency, whereas a fibroid is usually harder and has a noticeably different vascular architecture over its surface [Fig 3,4].

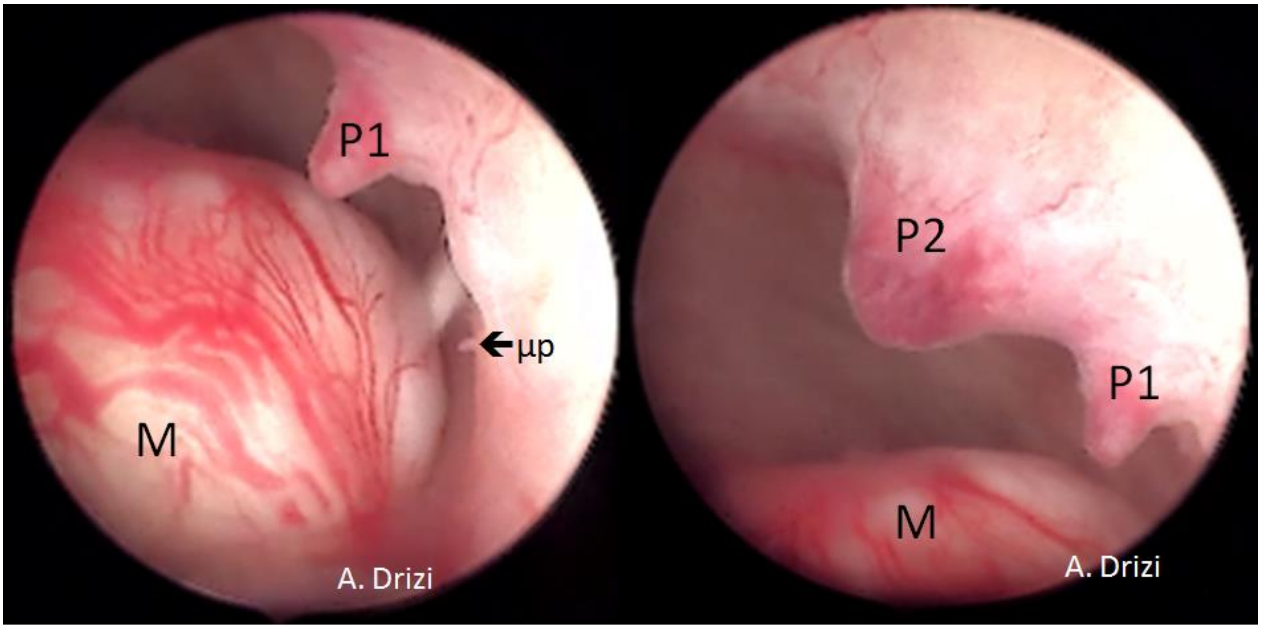

Figure 3. Submucous myoma located next to 2 endometrial mucous polyps: different hysteroscopic features. M: myoma; P: Polyp; 1: first; 2: second; µp: micropolyp. Images by A. Drizi

A gentle attempt to scrape off the endometrium over the mass with the tip of the telescope can also differentiate a polyp, whose base is friable and easily disturbed, from a myoma which does not move on touching, but sheds away its covering endometrium to expose the surface more distinctly [fig 3].

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Figure 4. Endometrial polyp. By S. Pisat.

Focal adenomyosis may also mimic a submucous myoma. However, some features differentiate adenomyosis from fibroids. Hysteroscopic signs of adenomyosis are: 1 Irregular endometrium with superficial openings; 2 irregular subendometrial myometrium (whorled, fibrotic, etc.); 3 absence of typical myometrial architecture during endometrial resection **[5].**

Atypical polypoid adenomyoma (APA) is another entity that looks like a submucous myoma, as a whitish mass protruding into the uterine cavity. It can be differentiated from a myoma only by histological examination, which shows atypical endometrial hyperplasia accompanied by nuclear enlargement and squamous metaplasia, with spindle cell hyperplasia in surrounding stromata [6].

Endometroid adenocarcinoma. The visual diagnosis is generally based on the presence of a gross distortion of endometrial cavity, because of focal or extensive nodular, polypoid, papillary, or mixed patterns of neoplastic growth. Focal necrosis, friable consistency, and atypical vessels are other features almost invariably associated with endometrial cancer and easily detected by hysteroscopic inspection [fig 5]

Pre operative imaging and fibroid mapping provides a very good assessment of each fibroid based on size, number, depth and location in the uterine cavity.

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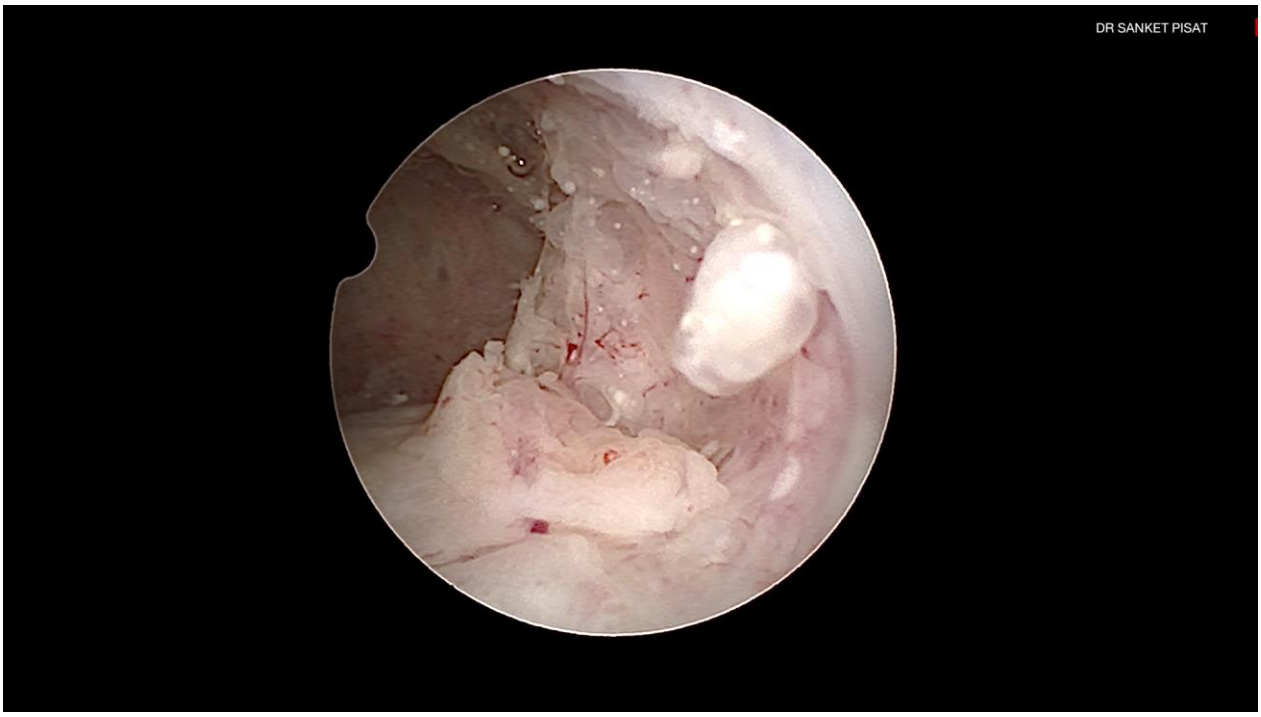

Figure 5. Endometroid adnenocarcinoma. Image by S. Pisat.

Various classifications such as the FIGO classification, the Wamsteker classification and the STEP W classification have been used to plan the surgery. Of these, the STEP W classification is the one that closely co relates to the intra operative findings **[2]** [table 1]**.**

Though these parameters are discussed independently, the final surgical decision is decided based on a cumulative assessment of all factors put together, not individually

a- Size of the myoma(s) : hysteroscopic myoma resection is, in principle, different from laparoscopic myomectomy as it deals with the volume of the fibroid which has to be removed piecemeal, vs laparoscopic myomectomy where the diameter, not volume of the fibroid has to be considered for removal. Consequently, a small increase in diameter by one or two centimetres does not significantly alter the difficulty level of the surgery in laparoscopic myomectomy. However, in hysteroscopic myoma resection, the volume of the fibroid (3.14 X radius^3) has to be removed. Hence, an increase in fibroid diameter by even one cm significantly increases the difficulty level and operative time.

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	Size (cm)	Topography	Extn of base	Penetration	Lateral wall	TOTAL
0	<2	Low	< 1/3	0	+ 1	
1	2 -5	Middle	1/3 to 2/3	<50 %		
2	> 5	Upper	> 2/3	> 50%		

Score	Group	Complexity & therapeutic options
0 to 4	I	Low complexity hysteroscopic myomectomy
5 to 6	II	High complexity hysteroscopic myomectomy- consider pre op GnRH use
7 to 9	III	Consider alternative to hysteroscopic technique

Table 1. The STEP W classification

For most surgeons, a size of 3 cm or less is an acceptable mass that can be removed without the risk of complications like fluid overload. However, this also depends on the depth of penetration of the myoma into the cavity. For fibroids that exceed 3 cm, a possibility of two stage surgery needs to be discussed with the patient before starting the case [fig 6].

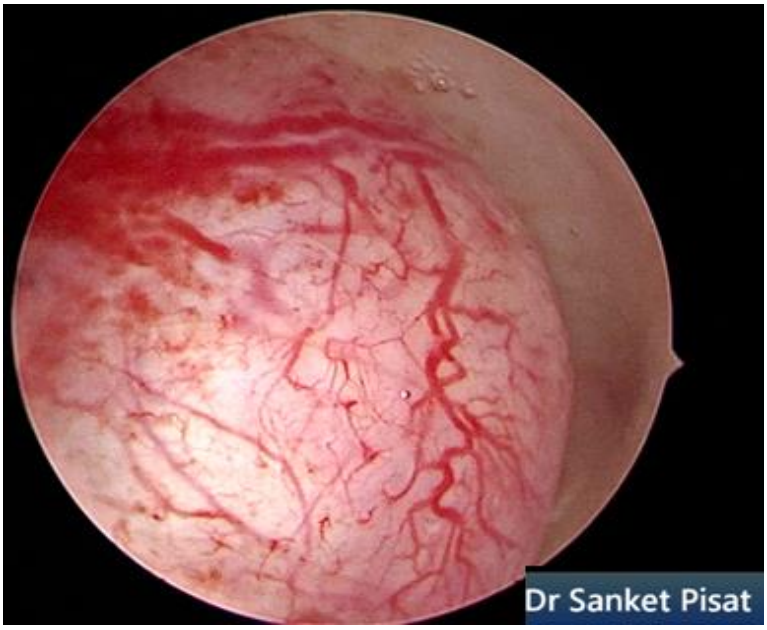

Figure 6. Large intra cavitary fibroid. By S. Pisat.

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b. **Number of fibroids:** The total number of fibroids to be removed determines the time and ease of surgery. A patient with two submucous myomas of 2 cm each will take as much time to remove as a patient having a single 4 cm fibroid. As in the case of large fibroids, the possibility of needing a two stage surgery must be explained beforehand.

c. **Location of fibroid in the uterine cavity**: a fibroid located lower down in the isthmus is more easily resectable than a fibroid located at or closer to the fundus. Likewise, it is easier to resect a fibroid located in the anterior and posterior wall than over the lateral wall

f.].

d. **Extension of the base**: a fibroid that covers one third or less of the wall is easier to resect than a fibroid having more than one third or two third of extension over the wall

e. **Depth of penetration**: The depth of penetration of the fibroid into the endometrial cavity is assessed. A fibroid that is more intra cavitary is easier to resect than a fibroid that is more deeply embedded into the uterine wall. Recognition of the fibroid pseudocapsule by means of its colour and texture, which is different from the myoma, allows the surgeon to define the end point of surgery [fig 7

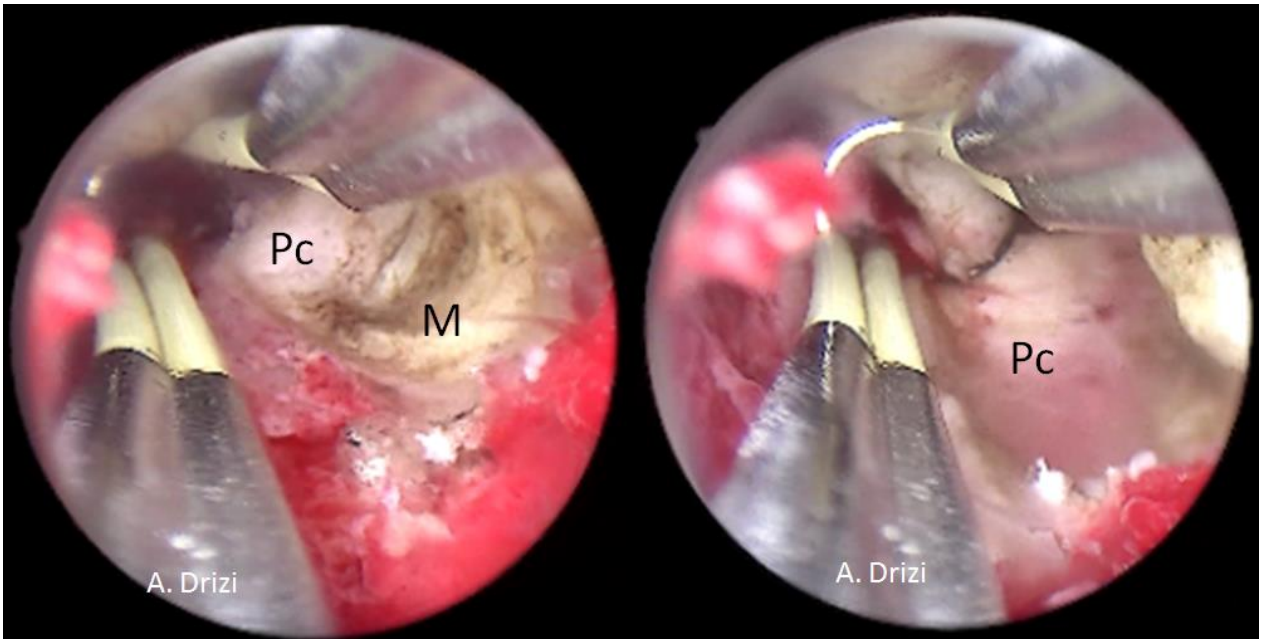

Figure 7. The aspect of the submucous myoma's pseudocapsula at hysteroscopy during resection. M: myoma; Pc: pseudocapsula. . Images by A. Drizi

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In these patients, a specific point to consider is whether the fibroid can be categorized into the type 2 to 5 category. This is a fibroid that has a bulge seen submucosally, but also extends up to the serosal margin because of its size. This fibroid requires removal by laparoscopy instead of hysteroscopy, and ensures that the entire mass can be removed in a single stage surgery, without the risk of dangerous fluid overload. Also, the endometrial lining is not subjected to extensive shaving by electrocautery, and hence post operative outcomes as regards fertility may be better [fig 8,9].

Figure 8. Submucous fibroid appearing as a type 3 at hysteroscopy. By S. Pisat.

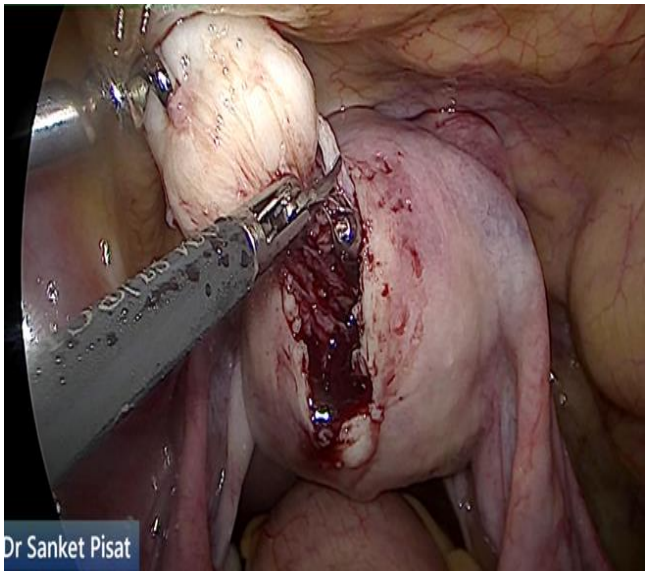

Figure 9. Submucous fibroid type 2 to 5, laparoscopically removed. Image by S. Pisat.

While performing the hysteroscopy, one important point to be noted is that the intra cavitary portion of the fibroid is always pushed away from the cavity by the pressure of the distending saline. Hence, while assessing the size and intra cavitary extension of the fibroid, it is vital to reduce the distension pressure to see how much the fibroid bulges into the cavity [fig 10,11]

The place of office hysteroscopy

Office hysteroscopy has expanded the role of hysteroscopy in patients with submucous fibroids. Almost all the parameters that were assessed using in patient hysteroscopy can now be evaluated in the outpatient department. The use of outpatient operative techniques like the OPIUMM technique have made treatment of deeper myomas easier and safer [8].

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Figure 10. Submucous myoma displaced outward due to distension pressure. By S. Pisat.

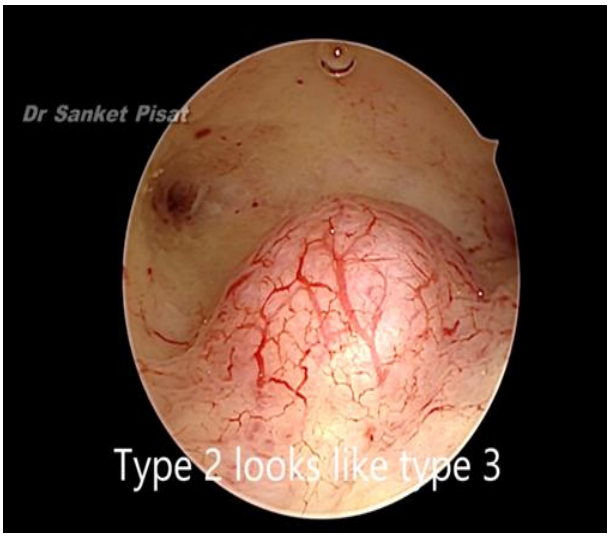

Figure 11. Fibroid bulging inward with reduced distension pressure. Image by S. Pisat.

Conclusion

The diagnosis of uterine myomas is accurately defined by imaging techniques thus allowing diagnostic hysteroscopy to be scheduled within the same session as surgery. It is important for every practitioner to grow awareness of the classic hysteroscopic features of myomas which are particularly helpful when differential diagnosis is suspected. In the case of myomectomy where the tumour is enucleated and left inside the cavity, diagnostic hysteroscopy additionally allows biopsy for histopathological confirmation.

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Fallopian tubes at diagnostic hysteroscopy

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The authors declare no conflict of interest.

Abstract

The Fallopian tubes are the passageway for the oocytes and sperms to meet and form an embryo to make its way to the uterus to implant. Infertility is a common problem of couples with reproductive age. Tubal abnormality is an important cause of infertility, accounting for 25%–35% of female infertility [1].

Tubal patency testing is important during infertility work up, before any assisted reproductive technique is performed. During hysteroscopy tubes are important guidance points as well, but during this procedure any lesion of the uterus or endometrium can be detected, not to mention the possibility for the tubal patency test.

Aim and method Our aim was to investigate the results of women who underwent selective pertubation via office hysteroscopy through a retrospective study. A total of 221 women were included in this retrospective study, who chose this method during their infertility work-up. The selective pertubation with office hysteroscopy was performed in an outpatient setting, without anaesthesia.

Results: Primary infertility in 158 cases (75.96 %), secondary infertility 43 (20.67 %), repeated abortions 3 (1.44 %) were the indications for office hysteroscopy. Regarding the selective perturbation test, we detected positivity (tubal blockage) in 61,32 % of the women. We divided patients into two groups. Under 30 years-old age unilateral occlusion had significantly higher prevalence (37.14%, p=0.001) compared to the group of patients over 30 years-old (31.40%) and in 19.77% of patients over 30 years-old had bilateral occlusion which is significantly higher than patients under 30 years-old (14.28%, P=0.0001). No complications occurred during the 221 diagnostic office hysteroscopies. During the follow-up questionnaire regarding all pregnancies 30 (88%) of patients had successful conception within one year. 46 women (92%) would suggest this method to other women.

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Conclusion: Our results suggest this novel method, selective pertubation with office hysteroscopy, which is an effective, accurate, minimally invasive method to investigate tubal patency, in outpatient circumstances to choose proper assisted reproductive techniques. This way the complications of general anesthesia or radiation (HSG) can be avoided. Due to the tubal flushing effect, this method can be therapeutic, as well. Moreover, with the examination of the uterine cavity, other uterine factors can be detected and treated so fertility can be improved as well.

Key words: Assisted reproduction (IVF, ICSI, IUI), Clinical Infertility Female, Diagnostic Techniques, Obstetrical and Gynecological, Hysteroscopy, Reproductive Surgery

Introduction:

Anatomic position, origin and function

The Fallopian tubes are important structures of the female genital tract, emerge from the posterior and superior part of the uterine corpus, supported by the broad ligaments. During the embryologic development Fallopian tubes, as well as the uterus, cervix, and upper third of the vagina, develop from the Müllerian ducts which originate from the mesonephric kidneys and mesonephros [2].

The lumen of the Fallopian tubes communicates with the uterine and the intraabdominal cavity. Each tube is divided into four parts named from the uterus: a broad interstitial section, with a narrowed lumen the isthmic part, again with a larger lumen the ampulla and the fimbria which is located at the end of the tubes with a spacious area.

The Fallopian tubes are the passageway for the oocytes and sperms to meet and form an embryo to make its way back to the site of implantation in uterus [3].

Fallopian Tubes during hysteroscopy

During hysteroscopic evaluation of the uterus the most important guidance points right after entering through the endocervical canal are the entrance of the Fallopian tubes both sides (Figure 1.). Having a panoramic view of the uterine cavity, tubal Ostia should be present at 2 and 10 o'clock location. The lack of the visualization of tubal ostium should warn the surgeon of false passage during the entrance, or severe intrauterine adhesions [4].

Fallopian tubes and infertility

Worldwide one of the leading methods, during the infertility workup should be the hysteroscopy to exclude the organic pathology of uterus and Fallopian tube in women. As tubal occlusion is one of the main causes of female infertility, evaluation of tubal patency is one basic point during the early phase of these infertility examinations. The relevance of diagnostic hysteroscopy, especially when performed in an outpatient "office" setting, in the evaluation

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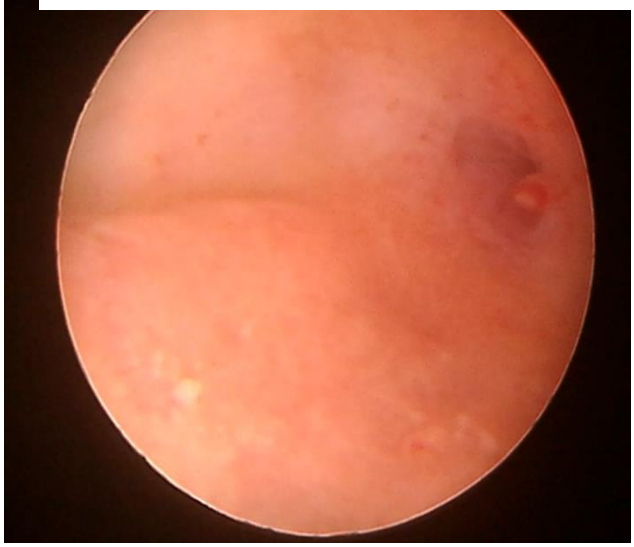
process of infertility has increased in the last years yet, not backed by evidence so far unfortunately. During hysteroscopy the uterine cavity and the entrance of the Fallopian tubes can be evaluated while dilated with distension media. Occlusion and therefore infertility can occur, if any endometrial or myometrial lesions, e.g., polyps and fibroids, block the entrance of the tubes (Figure 2.). With the help of operative tools such as resectoscope, scissors or HTRS, these lesions can be easily treated.

Figure 1. Right tubal ostium with some air-bubbles. Image by P. Török

Figure 2. Left tubal ostium with a small polyp at the entrance. Image by P. Török



While using fluid distension air can be injected into the uterine cavity and the movement of air bubbles can be followed through the hysteroscopic monitor. As an indirect sign, the escape of the air bubbles towards the ostia of the Fallopian tubes from the uterine cavity can be rated as a sign of tubal patency. Several studies have examined this phenomenon and assessed the accuracy of the bubble sign. Unfortunately, this sign means proximal patency of the tubes. In case of distal blockage there will be passage of air bubbles through the ostia. In case of hydrosalpinx or peri tubal adhesions the risk for a false-negative results are increased [5, 6, 7].

The gold standard for tubal patency test is the laparoscopic chromo-hydrotubation of the Fallopian tubes but still there are many disadvantages e.g., invasiveness, need of operating room, anaesthesia, missing from work, compared to the other hysteroscopic solution

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which is the office hysteroscopy-guided selective chromopertubation test. This method regarding the overall costs is less expensive, no need for anaesthesia, can be performed in an outpatient setting. A 2.7-mm optic is used for the evaluation with a 5.5-mm sheath (EMD Kft, Debrecen, Hungary). Vaginoscopic approach is used for the entrance to the cervical canal. As a distension media normal saline solution is used. The tip of a flexible, transparent plastic catheter is placed through the working-channel to each entrance of the Fallopian tubes. Through the catheter methylene blue dye is injected. If the catheter stained blue and no back-flow can be detected, view of the endometrium and uterine cavity remains clear, patent tube is diagnosed (Figure 3.). If the Fallopian tube is occluded, the uterine cavity becomes blue because of back-flow of the dye (Figure 4.). We can give lot confidence and credit for this method as specificity and sensitivity were estimated 82.1%, 83.3%. The accuracy of the test can be increased if the hysteroscopic evaluation is followed by a transvaginal ultrasound examination. So, the overall accuracy of this method is 82.9% with the laparoscopic method taken as reference [8, 9]. This diagnostic test, as others for patency test, can be therapeutic, as well. Due to the tubal flushing effect, endometrial detriments, sludges can be washed out of the tube, causing patency [10,11].

Material Method:

Our aim was to investigate the results of women who underwent selective pertubation with office hysteroscopy. In each case before and after the procedure 3D ultrasound was performed. A total of 221 women were included in this retrospective study, after signed informed consent and accepted ethical approval, who chose this method during their infertility work-up between 2016.11.01.-2022.12.29.

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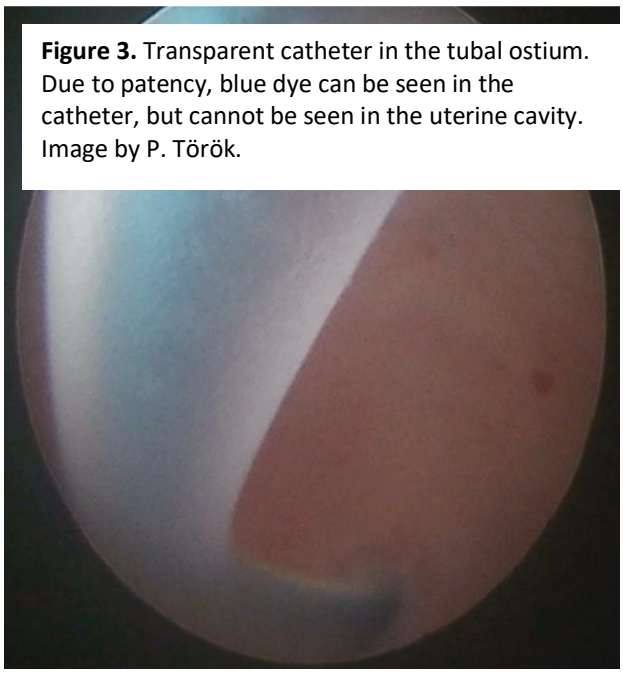

Figure 3. Transparent catheter in the tubal ostium. Due to patency, blue dye can be seen in the catheter, but cannot be seen in the uterine cavity. Image by P. Török.

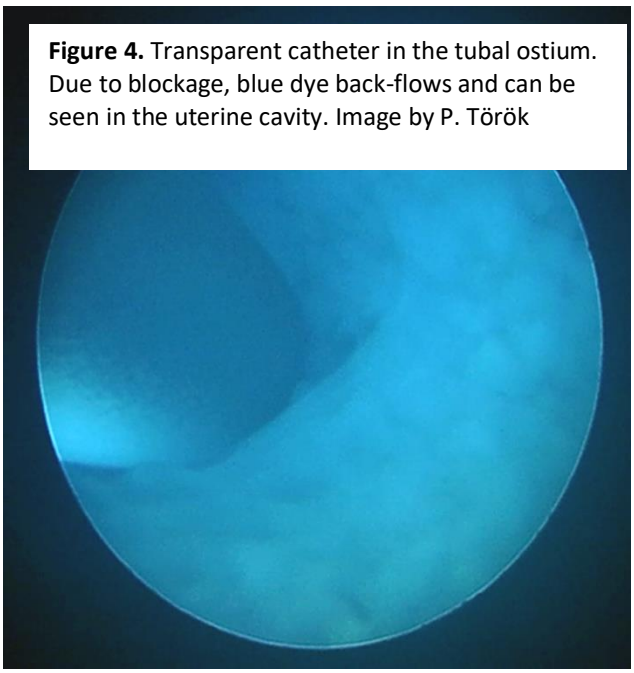

Figure 4. Transparent catheter in the tubal ostium. Due to blockage, blue dye back-flows and can be seen in the uterine cavity. Image by P. Török

For infertility we used the most common definition: no conception in more than 1 year (6 months above age 35), unprotected intercourses. As a follow-up, a questionnaire was submitted from 53 women after the procedure through phone call to evaluate post-procedure pregnancy and delivery.

Results:

Primary infertility 158 (in 75.96 %), secondary infertility 43 (in 20.67 %), repeated abortions 3 (in 1.44 %) were the indication for office hysteroscopy. Besides the infertility in 5 (2.40 %) cases, previous positive ultrasound result was the indication of hysteroscopy as well. The mean age of the patients was 33.4 ± 5.34 years, body mass index was 23.76± 4.60 (table 1). During the evaluation of uterine cavity 13 cases required polypectomy as well, 2 patients needed uterine myomectomy, in 3 cases septotomy was performed. Endometrial visualization and strawberry like endometrial surface of 43 cases indicated biopsy as well during the evaluation with office hysteroscopy, this way 15 chronic endometritis were detected.

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Age (years)	33.40 (±5.34)
Height (m)	166.89 (±6.38)
Weight (kg)	66.13 (±13.02)
Body Mass index (kg/m^2)	23.76 (±4.60)

Table 1. Data of women who underwent office hysteroscopy selective pertubation.

Regarding the selective perturbation test, we detected positivity (tubal blockage) in 61,32 % of the women, among them we explored unilateral occlusion 43,08 % of the cases and bilateral occlusion cases in 56,92 % of the patients. We divided patients into two groups. Under 30 years-old age unilateral occlusion had significantly higher prevalence (37.14%, p=0.001) compared to the group of patients over 30 years-old (31.40%). Regarding the bilateral occlusion, tests showed opposite results. In 19.77% of patients over 30 years-old had bilateral occlusion which is significantly higher than patients under 30 years-old (14.28%, P=0.0001) (table 2).

No complications occurred during the 221 diagnostic office hysteroscopy. During the follow-up questionnaire from 53 women 34 (68%) had at least one live birth since the procedure, out of them 5 (14%) women conceived spontaneously, 13 (38%) women had intrauterine insemination, and 16 women had successful ART. Regarding all pregnancies 30 (88%) of patients had successful conception within one year. 46 women (92%) would suggest this method to other women.

	Patients <30 years-old age	Patients >30 years-old age
Unilateral occlusion	37.14%	31.40%
Bilateral occlusion	14.28%	19.77%

Table 2. Results of office hysteroscopy selective perturbation tests regarding age-divided subgroups.

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Discussion:

Tubal factor contributes 30% of all female infertility, usually originate secondary due to tubal occlusion as a consequence of pelvic inflammatory diseases caused by several pathogens. Finding an accurate, cheap, easily available, painless method for diagnosis of tubal occlusion is crucial regarding the infertility work-up. Our results suggest office hysteroscopy, especially office hysteroscopy-guided selective chromopertubation method for evaluation tubal patency because this is an effective, reproducible, accurate, minimally invasive method to investigate tubal patency, with less or no pain in outpatient circumstances in order to choose appropriate assisted reproductive techniques to conceive. This way the complications of general anaesthesia or radiation (hysterosalpingography) can be avoided. With the accuracy of 82.9% compared to the gold-standard laparoscopic chromo-hydrotubation this method can be accepted as a first-line, out-patient test.

In our study we found bilateral blockage of the tubes significantly frequent (19.77%) in older (over 30 years old) subgroup compared to the younger (less than 30 years old) subgroup (14.28%). The diagnostic tubal patency test at the same time can be therapeutic, as well, caused by the tubal-flushing effect. Due to the feed-back of the patients, this method is acceptable and 92% of them is recommended to others. Moreover with the examination of the uterine cavity, visualization of the tubal Ostia, other factors, such as polyps, fibroids at the entrance von the tubes, or micropolyps, chronic endometritis can be detected and treated so fertility can be improve as well [12].

Conclusion:

Our results suggest this novel method, selective pertubation with office hysteroscopy, which is an effective, accurate, minimally invasive method to investigate tubal patency, in outpatient circumstances to choose proper assisted reproductive techniques. This way the complications of general anesthesia or radiation (HSG) can be avoided. Due to the tubal flushing effect, this method can be therapeutic, as well. Beyond the tubal patency with this method intrauterine pathologies, other causes of infertility could be ruled out or treated as well.

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Diagnostic Hysteroscopy in Retained Products of Conception (RPOC)

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The author declares no conflict of interest.

Abstract:

Retained Products of Conception (RPOC) refer to the tissue that remains in the uterus after a pregnancy loss. The diagnosis of RPOC can be challenging and often requires further investigation. This study aims to evaluate the efficacy of diagnostic hysteroscopy in detecting RPOC. A literature review was conducted to identify studies that utilized diagnostic hysteroscopy for the diagnosis of RPOC. The results of these studies were analyzed to determine the diagnostic accuracy, sensitivity, and specificity of hysteroscopy in detecting RPOC. The findings suggest that diagnostic hysteroscopy is a reliable and effective tool in the diagnosis of RPOC with a high diagnostic accuracy, sensitivity, and specificity.

Key words:

Abortion; Diagnostic Techniques; Hysteroscopy; Pregnancy Complications; Residual Products of Conception; RPOC

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Introduction:

Retained Products of Conception (RPOC) refer to the tissue that remains in the uterus after a pregnancy loss. RPOC can lead to complications such as infection, bleeding, and persistent pain (1). The diagnosis of RPOC can be challenging, particularly in cases where the products of conception are small or have been reabsorbed (2). Common diagnostic methods include clinical examination, ultrasonography, and laboratory testing (3) (figure 1). However, these methods are often insufficient for a definitive diagnosis, and further investigation is required (4).

Diagnostic hysteroscopy is a minimally invasive procedure that allows for visualization of the inside of the uterus using a hysteroscope (5). It has been utilized for various gynecological indications, including infertility, abnormal uterine bleeding, and uterine malformations (6). In recent years, the use of diagnostic hysteroscopy for the diagnosis of RPOC has gained increasing attention (7).

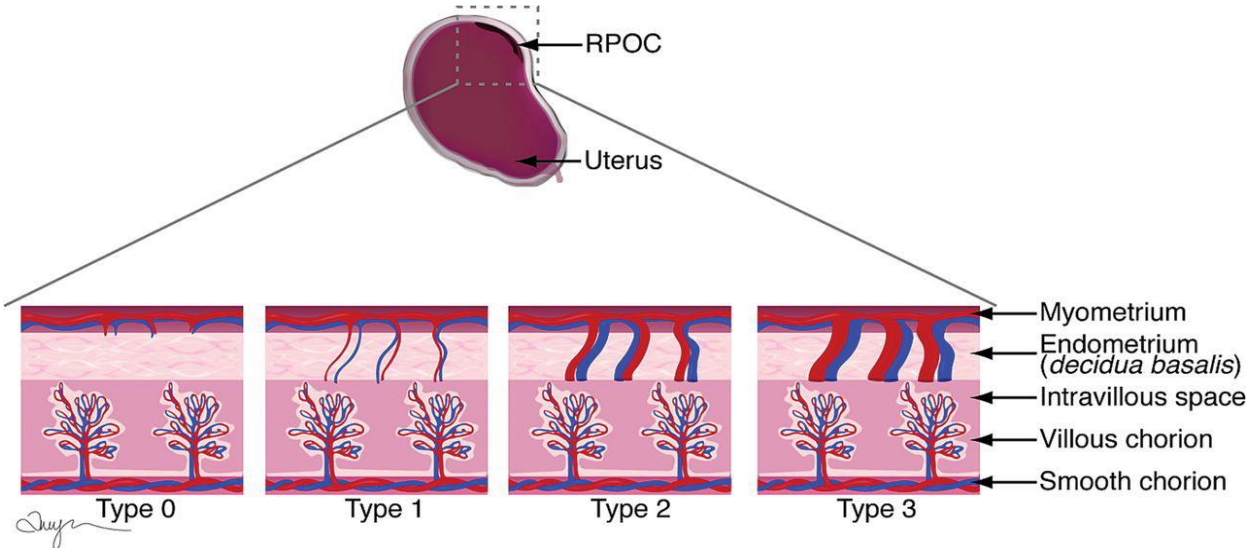

Figure 1. Drawings illustrate RPOC with various types of vascularity (types 0–3). The degree of vascularity is measured by comparing endometrial with myometrial blood flow at color Doppler US. (Courtesy of Amy Morris, Stanford University)

Objectives:

The aim of this study was to evaluate the efficacy of diagnostic hysteroscopy in detecting RPOC. A literature review was conducted to identify studies that utilized diagnostic hysteroscopy for the diagnosis of RPOC. The results of these studies were analyzed to determine the diagnostic accuracy, sensitivity, and specificity of hysteroscopy in detecting RPOC.

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Methods:

A systematic literature review was conducted to identify relevant studies that utilized diagnostic hysteroscopy for the diagnosis of RPOC. The search was performed in the PubMed and Cochrane Library databases. The keywords used for the search were “diagnostic hysteroscopy,” “RPOC,” and “retained products of conception.” The inclusion criteria were studies that utilized diagnostic hysteroscopy for the diagnosis of RPOC, with a sample size of at least 10 patients. The exclusion criteria were studies that utilized therapeutic hysteroscopy, case reports, and non-English language articles.

The results of the selected studies were analyzed to determine the diagnostic accuracy, sensitivity, and specificity of hysteroscopy in detecting RPOC. The diagnostic accuracy was calculated as the proportion of correct diagnoses (both true positive and true negative) made by hysteroscopy. The sensitivity was calculated as the proportion of true positive diagnoses made by hysteroscopy. The specificity was calculated as the proportion of true negative diagnoses made by hysteroscopy.

Results:

The search yielded a total of 20 articles, of which 13 were eligible for inclusion in the analysis. The studies included a total of 548 patients who underwent diagnostic hysteroscopy for the diagnosis of RPOC. The mean age of the patients was 32.6 years (range: 22-41 years). The diagnostic accuracy of hysteroscopy in detecting RPOC was found to be 97.2% (95% CI: 95.7-98.6%). The sensitivity of hysteroscopy in detecting RPOC was 98.1% (95% CI: 96.6-99.6%), and the specificity was 96.4% (95% CI: 94.0-98.8%).

Discussion:

The results of this systematic literature review suggest that diagnostic hysteroscopy is a reliable and effective tool in the diagnosis of RPOC (figures 2-5). The high diagnostic accuracy, sensitivity, and specificity of hysteroscopy suggest that it is a valuable diagnostic option for clinicians in cases where the diagnosis of RPOC is uncertain. This is particularly important given the potential complications that can arise from RPOC and the need for timely diagnosis and management.

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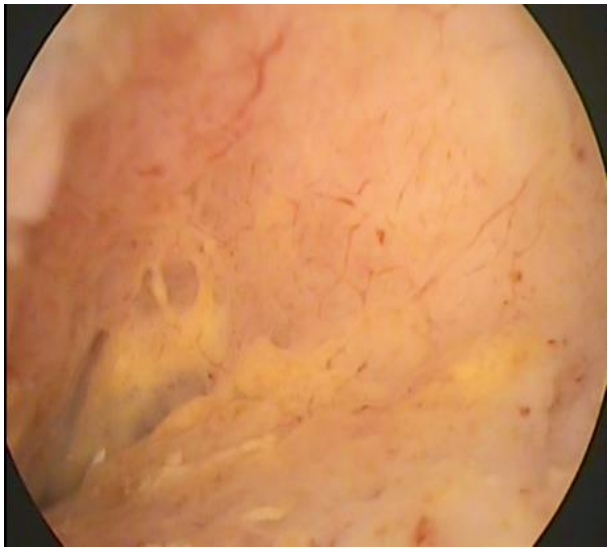

Figure 2. Hysteroscopic image shows RPOC Type 0. By L. Mikulàsek.

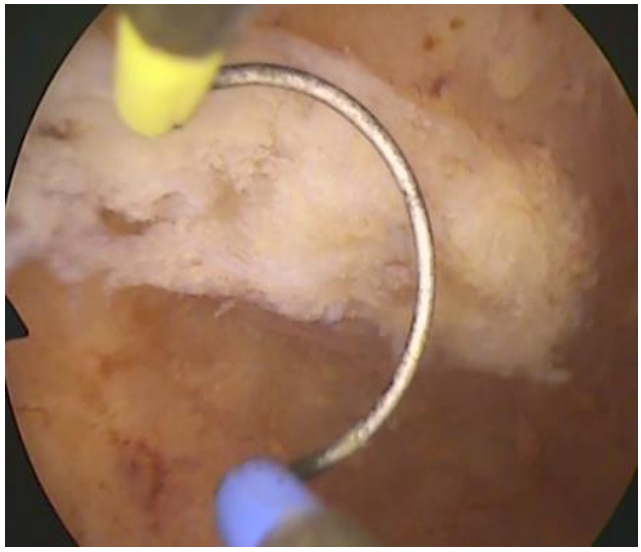

Figure 3. Hysteroscopic image shows RPOC Type 1. By L. Mikulàsek.

The use of diagnostic hysteroscopy for the diagnosis of RPOC has several advantages over other diagnostic methods. It allows for direct visualization of the inside of the uterus, which is especially useful in cases where the products of conception are small or have been reabsorbed. Additionally, hysteroscopy can be performed as a minimally invasive procedure, reducing the need for more invasive diagnostic methods such as dilation and curettage (D&C).

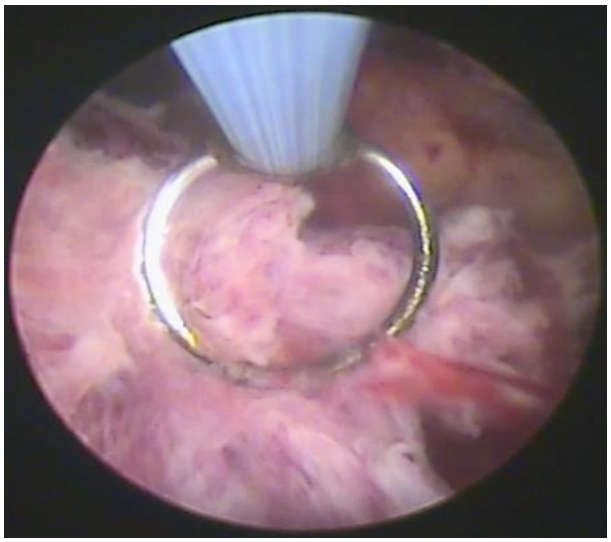

Figure 4. Hysteroscopic image shows RPOC Type 2. By L. Mikulasek.

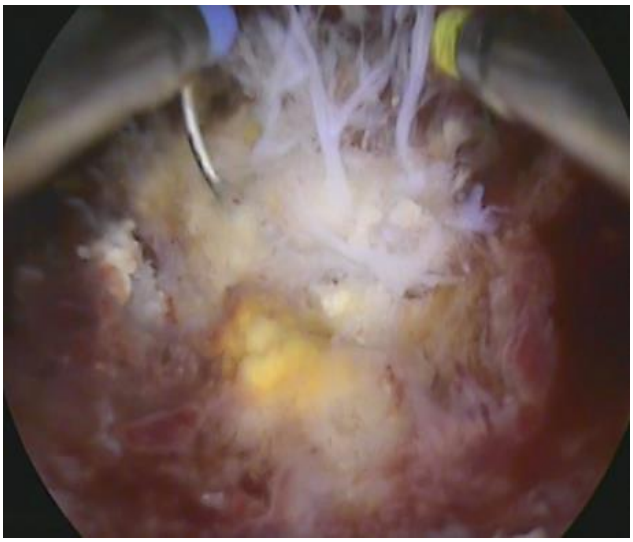

Figure 5. Hysteroscopic image shows RPOC Type 3. By L. Mikulasek.

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Conclusion:

Diagnostic hysteroscopy is a reliable and effective tool in the diagnosis of RPOC. The high diagnostic accuracy, sensitivity, and specificity of hysteroscopy suggest that it is a valuable diagnostic option for clinicians. However, it is important to consider the limitations of the procedure and weigh the potential risks and benefits for each individual patient. It is also important to plan the diagnostic hysteroscopy in the case of RPOC with the operative one as it allows resection and consequently the definitive histopathological diagnosis.

Further research is needed to further assess the clinical utility of diagnostic hysteroscopy in the diagnosis of RPOC.

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Title: Diagnostic hysteroscopy in intrauterine adhesions.

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Abstract

In this article we aimed to assess the role of diagnostic hysteroscopy in intra uterine adhesions. It is challenging to diagnose the severity of the disease in order to provide the effective treatment in cases with menstrual disturbances like hypomenorrhea and amenorrhea and infertility issues.

Methods and Outcome: In this article we provide a non-systematic review on the role of diagnostic hysteroscopy in evaluation of intra uterine adhesion and discuss it in detail. Hysteroscopy being the gold standard diagnostic and therapeutic modality for intra uterine adhesions outweighs the other modalities like hysterosalpingography, transvaginal ultrasound, sono-hysterography and MRI. Also, there are various hysteroscopy-based classification systems available which have been discussed in chronological order. The

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American Fertility Society (AFS) classification which includes clinical picture along with hysteroscopic findings is by far most widely accepted among various classification systems.

Conclusion: Hysteroscopy is by far the best diagnostic tool to diagnose the intra uterine adhesions and also to assess its severity in the real time. The diagnosis and treatment can be provided in the same setting with this cost-effective and time saving procedure.

Key words:

Diagnostic hysteroscopy; intrauterine adhesions (IUA), classification of IUA.

Introduction:

Intra Uterine adhesions (IUAs) designate bands that are formed inside the uterine cavity and maybe due to a multitude of causes. Following any uterine procedure, fibrous bands that are formed in the endometrial cavity, are termed as IUAs It can be in the form of thin strings of tissue or it can be so severe that it may obliterate the uterine cavity completely. Infertility, menstrual abnormalities, recurrent miscarriages, and lower abdominal pain are its clinical sequelae. H. Fritsch in 1894 first described amenorrhea linked with IUA in a woman who underwent postpartum curettage [1]. Later, J.G. Asherman in 1948 and 1950 published two such reports [2,3] on the etiology and the frequency of intrauterine adhesions and since then the term Asherman's syndrome has been used, oftentimes improperly and interchangeably with IUA. However, it is important to highlight the clear distinction that Asherman syndrome is only about the severe IUAs subsequent to pregnancy-related trauma. All other cases come under the broader term of Intrauterine Adhesions [4]. The presenting symptoms associated with IUA (also known as synechiae) are usually infertility, menstrual abnormality, recurrent pregnancy losses, or abnormal placental attachment [5,6].

Among women with intrauterine adhesions, the most common symptom is infertility, affecting approximately 43% [5,7]. Menstrual disturbances like amenorrhea and hypomenorrhoea are also common presentation, nonetheless the term Asherman's syndrome is technically interchangeable with secondary amenorrhea [5,7]. Women having intrauterine adhesions accounts for 14% chances of having recurrent pregnancy loss. Disorders of placental attachment such as placenta previa and accreta are comparatively rare (1%) [5,7].

It has always been challenging to make the diagnosis of IUAs and Asherman’s syndrome [8,9]. Recently, the advent of various diagnostic

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modalities and increased consciousness of the condition have directed towards a more definitive diagnosis and management of this condition [10]. Hysteroscopy is presently the gold standard diagnostic and therapeutic modality for the IUAs, as it provides clear view of the uterine cavity without any abdominal incision [11-14]. In this article we shall be reviewing various articles on the role of diagnostic hysteroscopy in evaluation of IUA and discuss it in detail.

Material Method:

In this article we provide a non-systematic review on the role of diagnostic hysteroscopy in evaluation of intra uterine adhesion and discuss it in detail. Hysteroscopy being the gold standard diagnostic and therapeutic modality for intra uterine adhesions outweighs the other modalities like hysterosalpingography, transvaginal ultrasound, sono-hysterography and MRI. Also, there are various hysteroscopy-based classification systems available which have been discussed in chronological order. The American Fertility Society (AFS) classification which includes clinical picture along with hysteroscopic findings is by far most widely accepted among various classification systems.

Results and discussion:

However, the correct diagnostic scheme (Figure 1) for IUAs should begin from clinical suspicion and ultrasound imaging and, consequently, confirmed with hysteroscopy, or other modalities such as hysterosalpingography (HSG), magnetic resonance imaging (MRI) or sonohysterography (SHG) where hysteroscopy facilities are not available [8].

Vaginoscopic method introduced by Stefano Bettocchi in the year 1997 is a no touch technique, which is a preferred technique these days as it has various advantages as compared to the conventional hysteroscopy (steps depicted in Figure 2).

Hysteroscopy is an excellent tool to identify the intrauterine adhesions and to assess its severity as depicted in figures 3, 4, 5.

Prognosis can also be assessed by evaluating the proportion of healthy endometrial tissue.

Intravaginal Misoprostol (prostaglandin E1) may be given a night before the procedure in a few selected cases with cervical stenosis to ensure an easy dilatation of cervical canal [15,16].

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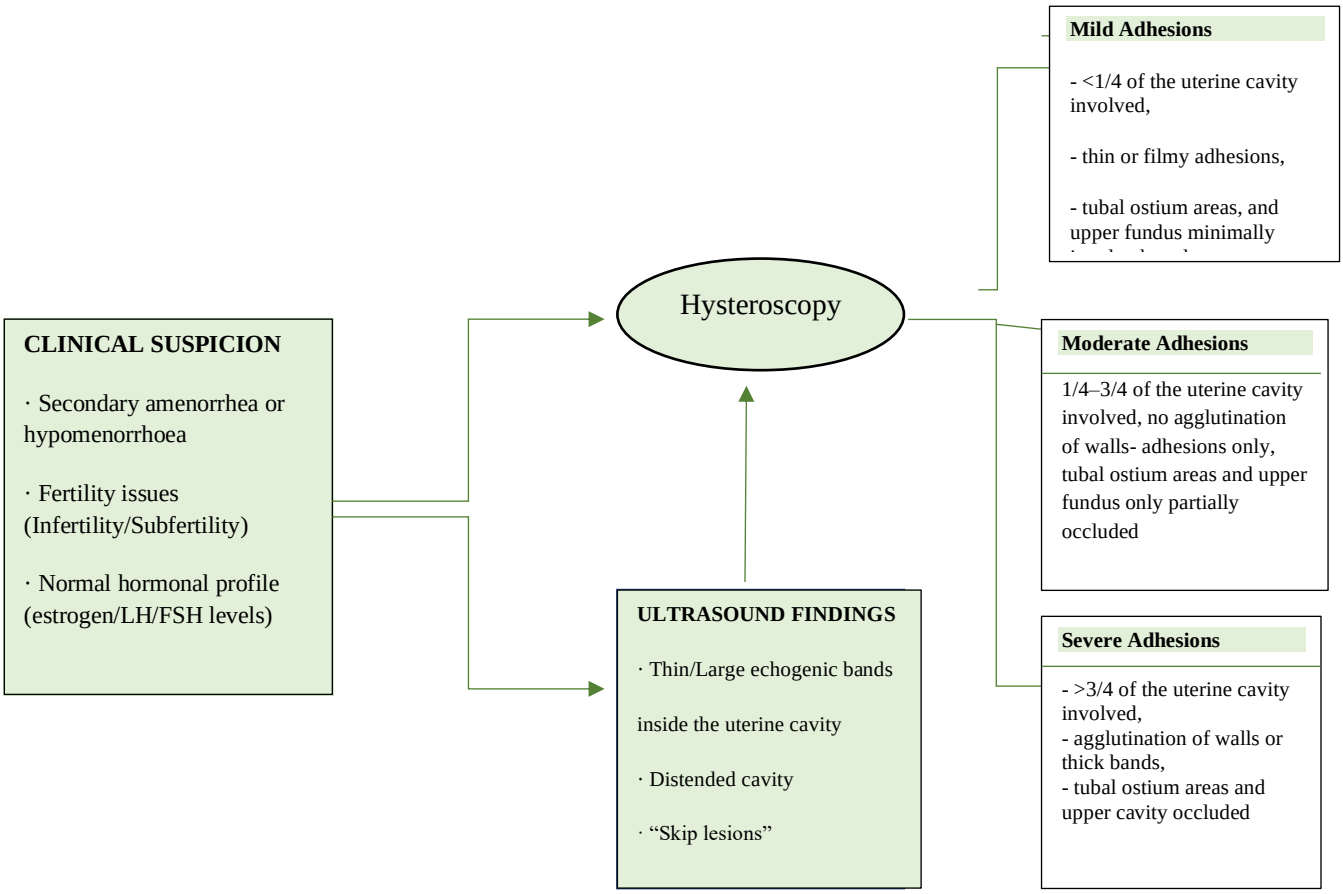

Figure 1. Diagnostic scheme for IUAs.

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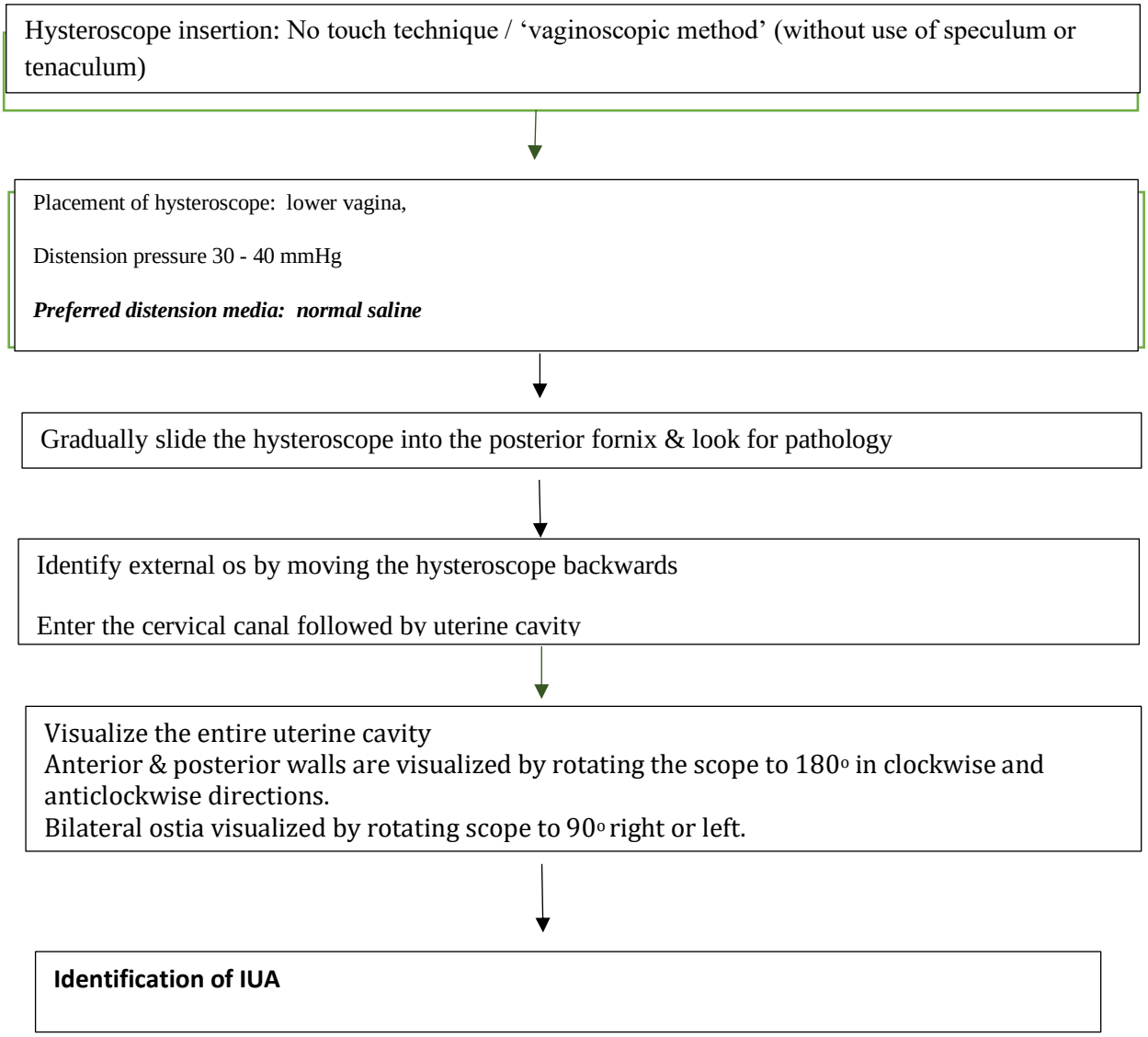

Figure 2. Steps to identify IUA on office hysteroscopy.

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Figure 3 depicts normal uterine cavity in comparison to IUA where adhesion can be mucosal variety or fibromuscular in nature. Mucosal adhesions simulate the surrounding endometrium pink in colour whereas fibromuscular adhesions are thicker and white in colour (Fig 4, 5).

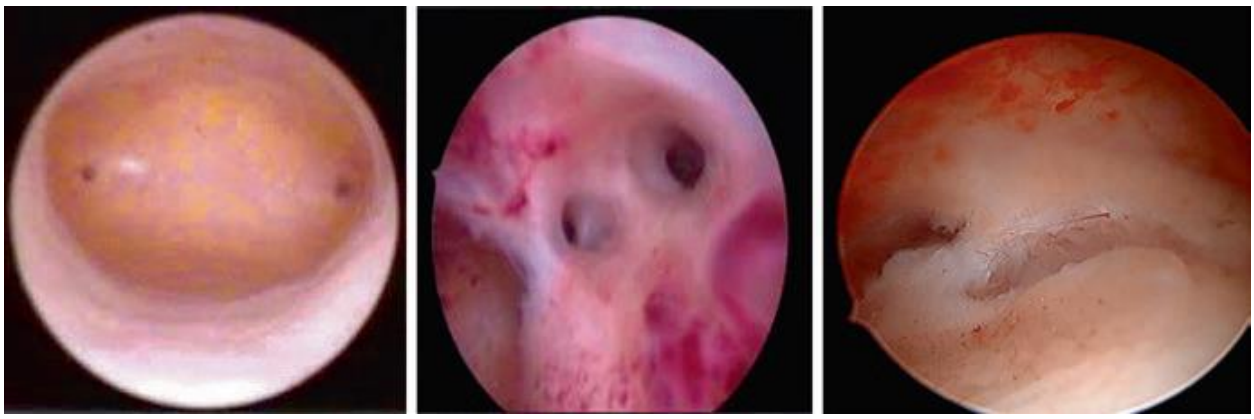

Figure 3. From left to right: normal cavity; mucosal adhesions; fibromuscular adhesions.

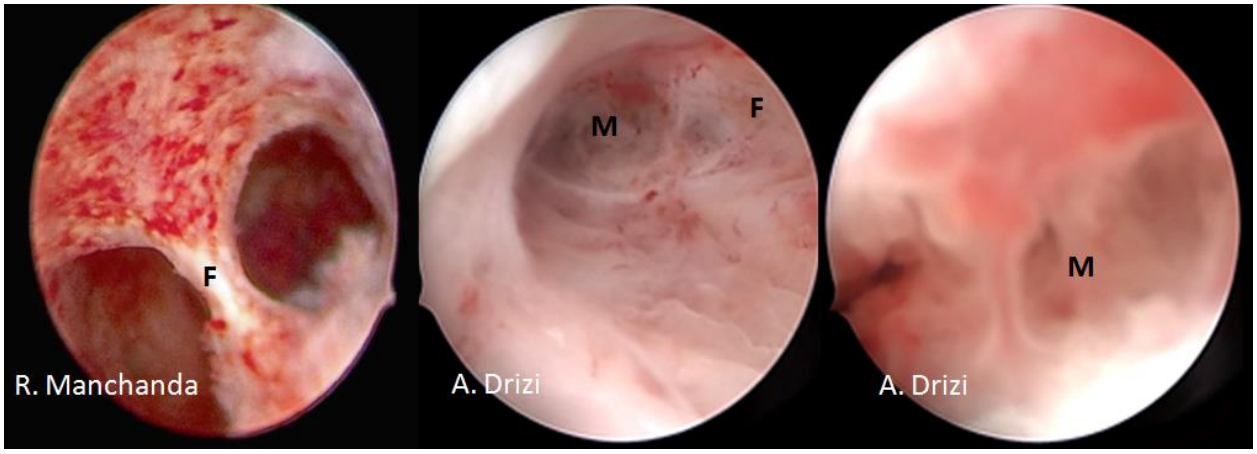

Figure 4. Isthmic adhesions. F: fibrous; M: mucosal

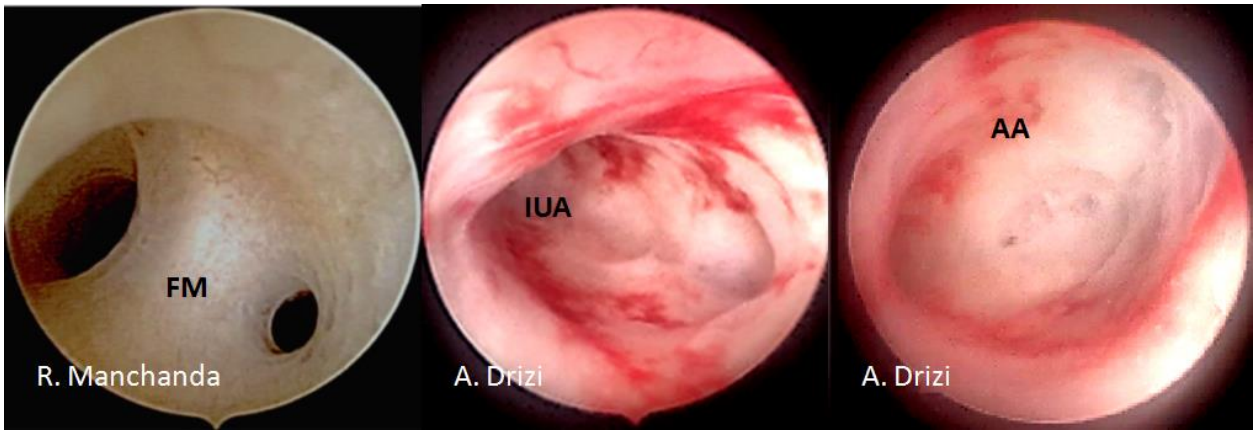

Figure 5. Thick adhesions. FM: fibro-muscular; IUA: Intrauterine adhesions; AA: After adhesiolysis.

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Classification systems:

There is a need to classify IUAs (as depicted in Table 1) so that it can serve as a guide to the prognosis after a treatment, which in itself is linked to the disease severity [17].

Classification	Year	Summary of classification
March [18]	1978	They were the first to classify IUA as minimal, moderate, or severe based on hysteroscopic assessment of the severity of uterine cavity involved.
Hamou [19]	1983	IUAs were classified as isthmic, marginal, central, or severe based on hysteroscopic assessment
Valle [20]	1988	IUAs were classified as mild, moderate or severe based on hysteroscopic assessment and extent of occlusion (partial or total) at HSG
American Fertility Society [22]	1988	Complex scoring system of mild, moderate and severe IUAs based on extent of endometrial cavity obliteration, appearance of adhesions, and patient menstrual characteristics based on hysteroscopy or HSG assessment
European Society for Hysteroscopy [23]	1989	Complex system classifies IUAs as grades I through IV with several subtypes based on a combination of hysteroscopic and HSG findings and clinical symptoms
Donnez and Nisolle [21]	1994	IUAs were classified into six grades based on their location determined by hysteroscopy or HSG and postoperative pregnancy rate being the primary clinical outcome
Nasr [24]	2000	Complex system generating a prognostic score by incorporating menstrual and obstetric history with findings at hysteroscopic assessment
MEC [25]	2016	Simple and easy to use system dividing AS into mild, moderate, and severe grade based on the extent of uterine involvement at hysteroscopy

Table 1. Various hysteroscopy-based classification systems for IUAs.

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March classification. March et al. in 1978 were the first ones to categorize IUAs based on hysteroscopic findings into minimal, moderate, and severe. The criteria used to grade the severity of IUAs was extent of adhesions present in the endometrial cavity and the degree of its occlusion. This classification system is still used because it is simple to use and easy to remember (Table 2.1). However, the shortcoming of this classification system is that there is no correlation with clinical symptoms and the post-treatment success was not defined [18].

Classification	Involvement
Severe	>3/4 of the uterine cavity involved, agglutination of walls or thick bands, tubal ostium areas, and upper cavity occluded
Moderate	1/4–3/4 of the uterine cavity involved, no agglutination of walls-adhesions only, tubal ostium areas and upper fundus only partially occluded
Minimal	<1/4 of the uterine cavity involved, thin or filmy adhesions, tubal ostium areas, and upper fundus minimally involved or clear

Table 2.1. Detailed classification of Intra uterine adhesions by March, 1978.

In 1983, Hamou et al. also included the extent and histologic nature of the adhesions as well as the evaluation of the surrounding glandular endometrium along with the degree of cavity distortion. (Table 2.2) [19].

The three types of adhesions described in his study are as follows:

- **Endometrial adhesions:** white, vascularization similar to the surrounding endometrium
- **Fibrous or connective tissue adhesions:** transparent, bridge-like and poorly vascularized
- **Myometrial adhesions:** highly vascular and extensive adhesions

The different types of adhesions identified were as follows:

- **Mild:** filmy adhesions composed of endometrial tissue causing partial or complete endometrial cavity occlusion.
- **Moderate:** fibromuscular adhesions, made up of endometrium causing partial or total occlusion of the endometrial cavity, can bleed on adhesiolysis.
- **Severe:** dense connective tissue adhesions, lack endometrial tissue and causing partial or total occlusion of the endometrial cavity, not likely to bleed on adhesiolysis.

DOI: 10.36205/trocar1.2023011

Location of the adhesions	Isthmic Marginal Central
Size of the adhesions	<1 cm2 >1 cm2
Type of adhesions	Endometrial adhesions Fibrous/ connective tissue adhesions Myometrial adhesions

Table 2.2. Classification of Intra uterine adhesions by Hamou, 1983

In an attempt to reduce the shortcomings of the previous classification systems, in 1988, Valle et al. suggested that success of treatment, identified by improvement in menstrual pattern, and reproductive outcomes, also had to be correlated with the severity of disease. This classification system thus included both the extent of endometrial cavity involvement as well as the type of adhesions [20] (Table 2.3).

Type of adhesion	-Mild -Moderate -Severe
Extent of uterine cavity occlusion	-Partial -Total

Table 2.3. Classification of Intra uterine adhesions by Valle, 1988.

Donnez and Nisolle classification. In 1994, Donnez and Nisolle re-emphasized the importance of using HSG in the classification of AS along with hysteroscopic finding and proposed a classification system based on both modalities. They broadly divided AS into three groups and six subgroups depending on the type of adhesion and the extent of uterine involvement as described in Table 2.4 [21].

The American Fertility Society (AFS) introduced a comprehensive classification system that became the most widely accepted IUAs classification system across the globe. It included the clinical symptoms (menstrual pattern) as an indicator of disease severity, which was considered important as it gives an estimate about the amount of endometrium which was available for potential regeneration post-adhesiolysis and serves as an important marker

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for defining the prognosis post-treatment, thus helping in pre-treatment patient counselling. Scoring points (1–3) were given to each of the included characteristics and staging of AS was done (stage I/II/III: mild/moderate/severe) according to the score obtained. Additionally, a prognostic score to each patient was for the first time assigned by a classification system and hence it became a more objective way of classification (Table 2.5) [22].

Degree	Location
I	**Central adhesion** a. Thin filmy adhesion (endometrial adhesions) a. Myofibrous (connective adhesions)
II	**Marginal adhesions** (always myofibrous or connective) a. Wedge like projection a. Obliteration of one horn
III	**Uterine cavity absent on HSG** a. Occlusion of the internal os (upper cavity normal) a. Extensive coaptation of the uterine walls (absence of the uterine cavity, true Asherman's syndrome)

Table 2.4. Classification of Intra uterine adhesions by Donnez and Nisolle, 1994.

Characteristics			
Extent of cavity involved	<1/3 1	<1/3–2/3 2	>2/3 4
Type of adhesions 1 2 4	Flimsy 1	Filmy and Dense 2	Dense 4
Menstrual pattern Normal Decreased Amenorrhoea 0 2 4	Normal 0	Decreased 2	Amenorrhoea 4
Prognostic classification: HSG score Hysteroscopy score Stage I (Mild) 1–4 Stage II (Moderate) 5–8 Stage III (Severe) 9–12			

Table 2.5. Classification of Intra uterine adhesions by American Fertility Society (AFS), 1988.

DOI: 10.36205/trocar1.2023011

Another classification system was proposed by the European Society of Hysteroscopy (ESH) in 1989, incorporating the menstrual pattern of women with IUA (as per table 2.6). However, the reproductive outcome of patients, which is one of the important aspects in cases of IUA, was not included. Another disadvantage of this classification system was that, despite it being a very comprehensive system for grading, its complexity makes it difficult to remember and use in clinical practice, thus limiting its utility [23].

Grade	Extent of intrauterine adhesion
I	Thin or filmy adhesion The adhesions are easily broken using only the hysteroscope sheath The cornual areas are normal
II	Single firm adhesion Connecting separate parts of the uterine cavity Visualization of each tubal ostium is possible Cannot be broken by hysteroscope sheath alone
IIa	Occluding adhesions only in the region of internal cervical os The upper uterine cavity normal
III	Multiple firm adhesions Connecting separate parts of the uterine cavity Unilateral obliteration of tubal ostium areas
IIIa	Extensive scarring of the uterine cavity with amenorrhea or decreased menstrual flow
IIIb	Combination of III and IIIa
IV	Extensive firm adhesions with agglutination of the uterine walls At least both tubal ostia areas are occluded

Table 2.6. Classification of Intra uterine adhesions by European Society of Hysteroscopy (ESH) 1989.

Nasr classification. Nasr et al. (2000) described a very comprehensive scoring system including the clinical symptoms (both menstrual pattern and reproductive outcomes) of the patients and the hysteroscopic findings along with providing a prognostic correlation as described in Table 2.7.

This system gives greater emphasis on the type of adhesions and the ability to visualize the tubal ostium over the involvement of the rest of the endometrial cavity.

DOI: 10.36205/trocar1.2023011

	Scoring
Hysteroscopic findings	
Isthmic fibrosis	2
Filmy adhesions few excessive (i.e.1/2 of the cavity)	 1 2
Dense adhesions single band multiple bands (i.e .1/2 of the cavity)	 2 4
Tubal ostium both visualized only one visualized both not visualized	 0 2 4
Tubular cavity (glove finger appearance) (sound less than 6)	10
Menstrual pattern Normal Hypomenorrhea Amenorrhea	 0 4 8
Reproductive performance Good obstetric history Recurrent pregnancy loss Infertility	 0 2 4
Score of 0–4: Mild →Good prognosis. Score of 5–10: Moderate → Fair prognosis. Score of 11–22: Severe → Poor prognosis.	

Table 2.7. Classification of Intra uterine adhesions by Nasr, 2000.

Adhesions were pathologically classified into three categories: filmy/dense/tubular. The latter, which is the most severe form of the disease, indicates dense adhesions obliterating the entire uterine cavity, thereby obscuring both the tubal ostia. Isthmic fibrosis was identified as a separate entity and was given special importance as it could initiate a neuroendocrine reflex and cause endometrial deactivation and amenorrhea even when the rest of the cavity is free of adhesions [24].

MEC classification. In 2016, the Manchanda's Endoscopic Centre (MEC) classification system

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was proposed in India, which categorized IUAs as mild, moderate, and severe disease owing to the extent of the endometrial cavity involvement. It encompasses both dense and flimsy adhesions in all categories. Its advantage is of being relatively simple and easy to use in clinical practice [25] (Table 2.8).

Grade	Category	Characteristics
Grade 1	**Mild**	Less than one-third of the uterine cavity is obliterated (filmy/dense adhesions)
Grade 2	**Moderate**	1/3–2/3 of the uterine cavity obliterated (filmy/dense adhesions)
Grade 3	**Severe**	More than two-thirds of the uterine cavity obliterated (filmy/dense adhesions)

Table 2.8. MEC classification of Intra uterine adhesions.

The reproductive outcomes based on this classification system were correlated with the severity of the adhesions in a retrospective analysis performed in 2018 by Sharma et al., who reported an increased number of live births after adhesiolysis in the moderate and severe categories of adhesions. The direction and degree of adhesiolysis performed by hysteroscopy were guided by preoperative assessment of myometrial thickness of fundal, anterior, and posterior uterine walls using the 'RR' method in this study [26].

The 'RR method' is named after the two main authors of this paper and refers to the measurement of myometrial thicknesses both at the fundus of the uterus and at anterior/posterior uterine walls, that guides the amount and the direction of hysteroscopic adhesiolysis [26].

Conclusion:

It is necessary to evaluate the extent of intra-uterine adhesions, in order to select the best treatment option in managing menstrual and infertility problems and analysing the postoperative success of adhesiolysis, hence hysteroscopic classification systems are useful. By and large AFS classification is the most widely accepted among these scoring systems which is a clinic-hysteroscopic classification. MEC classification is the most recent classification system, which is hysteroscopy-based scoring system that has been developed in 2016 in India and is relatively simple and easy to implement

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under clinical settings. A universally agreed upon classification system is needed to predict post-treatment reproductive outcomes according to the severity of the condition. MRI is not a cost-effective diagnostic tool for the IUAs. Hysteroscopy is cost-effective tool to get a real time view of the uterine cavity which helps in accurate description of intrauterine adhesions and assesses its severity and treatment can also be provided in the same setting hence it is time saving procedure as well.

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Diagnostic hysteroscopy for congenital anomalies of the female genital system.

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Abstract

Congenital anomalies of the female reproductive system are commonly seen in 4-6% of women. [1] These may be responsible for infertility and recurrent pregnancy loss. With the advent of three-dimensional (3D) ultrasound, many of these anomalies can be reliably diagnosed without performing any invasive techniques. Yet, hysteroscopy when combined with imaging provides a way to confirm the diagnosis and treat these patients with optimal reproductive outcomes.

This nonsystematic review article aims to define the role of hysteroscopy in diagnosis and classification of these anomalies, along with addressing some treatment dilemmas that arise when these conditions are encountered in every day practice

Key words:
Uterine malformations; diagnostic hysteroscopy; classifications.

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Introduction

The prevalence of congenital uterine anomalies is reported to be 4.3–6.7% in the general population, 3.4%–8% in the infertile population, and 12.6–18.2% of those with recurrent miscarriages [1]

According to the findings of this review the commonest anomalies follow the order of arcuate, septate and bicornuate at a ratio of approximately 17:7:1 [2]

Septate uterus is the most common uterine anomaly in the infertile population (3.9%), while the arcuate uterus is the most common anomaly in the general population and in those with recurrent miscarriage. The prevalence of uterine septum and arcuate uterus in infertile patients varies in the literature, but it is estimated to be 3.9% and 2.1% respectively [2].

Classification

Congenital uterine anomalies are classified, according to the CONUTA classification from U0 to U6 according to the deformity [3] [table 1].

	CLASS	SUBCLASS
U0	Normal uterus	
U1	Dysmorphic uterus	a. T shaped b. Infantilis c. Other
U2	Septate uterus	a. Partial b. Complete
U3	Bicorporeal uterus	a. Partial b. Complete c. Bicorporeal septate
U4	Hemi Uterus	a. With rudimentary cavity b. Without rudimentary cavity
U5	Aplastic uterus	a. With rudimentary cavity b. Without rudimentary cavity
U6	Unclassified	

Table 1. CONUTA classification of congenital uterine anomalies

A variety of techniques has been utilized for assessing the uterine cavity such as hysterosalpingography (HSG), two dimensional (2D) trans vaginal sonography (TVS), saline infusion sonography, three dimensional TVS (3D TVS) and even magnetic resonance imaging (MRI) [4].

3D TVS, a new technique of imaging, has the ability to register all three imaging planes

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simultaneously as well as visualize the surfaces three dimensionally.[8,9] It thus provides a unique diagnostic tool for noninvasive visualization of the uterine morphology as well as the diagnosis of congenital uterine anomalies [4].

MRI also provides detailed information on the uterovaginal anatomy, particularly in the study of the external profile of the uterine fundus and the cavity shape, and it also allows visualization of the septum within the cavity

Role of Ultrasonography (USG) and Magnetic Resonance Imaging (MRI).

The clinical and imaging diagnosis must be certain before proceeding with an invasive (even diagnostic) surgical intervention

Patient Preparation

The patient is preferably scheduled for surgery in the early proliferative phase of the menstrual cycle. This ensures that the endometrial lining is at its minimum thickness, and smaller shape defects like an arcuate uterus, or a unilateral convergent wall (the 7- shaped uterus) are not missed during the primary examination because of being obscured by the thick endometrium.

Hysteroscopy is best performed using a 2.9 mm or 1.9 mm hysteroscope that allows easy entry into the uterine cavity. The administration of vaginal misoprostol 400 µg, 4 hrs before the procedure may aid in an easy entry into the cavity, although there is no evidence to support its routine use in hysteroscopy [5].

Hysteroscopic approach

Entry

The preferred route of entry into the uterine cavity is by using the vaginoscopy- hysteroscopy technique. In patients undergoing an office procedure, this is the only available technique [6]. However, even in patients who are being operated upon under anaesthesia, performing a vaginoscopy – hysteroscopy and 'entering under vision' is equally important. This ensures that the entire vagina, its fornices and the cervical anatomy, along with the external os is clearly visualized before an entry is made into the cavity. This ensures that even minor defects are not missed out. Needless to say, vaginoscopy is an adjunct to, and does not replace a thorough per speculum and per vaginal exam.

Some of the anomalies/ abnormalities that could be detected at this stage are

1. Complete vaginal septum – associated with a complete uterine + cervical septum

   Both halves of the vagina, and both hemi cervices are inspected after distending each hemi vagina with the distension medium. The telescope is inserted in each hemi cavity and both ostia visualised

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2. Transverse vaginal septum – possibly associated with agenesis of the lower cervix / upper vagina. A pinpoint opening of the transverse septum may be seen, though in most cases it is too small to be negotiated with a telescope
3. Concomitant puckering and nodularity of the posterior fornix suggesting recto vaginal septum endometriosis – frequently associated with a non communicating functional hemi uterus and pelvic endometriosis
4. A pinpoint external os – in patients with hypoplastic uterus
5. Cervix completely flushed to the vaginal wall

The view from the internal os

Once the internal os has been negotiated, the first look into the cavity provides a wealth of information

The surgeon must carefully inspect the fundus, lateral walls and both ostial openings from the vantage point of the internal os. On inspection, a 'normal' uterus should have the following features (fig 1)

1. The fundus is usually curved slightly inwards, rather than completely flat. Subsequently, the area between the two ostia appears slightly elevated and projecting into the cavity
2. The two ostia are equidistant from the midline
3. Both ostia are seen in one single view (not a very consistent finding)
4. If the two ostia are not seen together in a single frame, each ostium is at least visible from the internal os when the light cable is tilted from the 6 O'clock to the 3 and 9 O'clock positions
5. The overall cavity appears 'spacious'. This is a subjective assessment, learnt over a period of time after performing a number of cases

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Figure 1. Normal uterine cavity (U0). By S. Pisat.

Any variations to this anatomy should raise the suspicion of a uterine anomaly. Of course, the hysteroscopy findings must complement, and not dispute the diagnosis that has been made on imaging pre operatively

a. The Septate/ arcuate Uterus (Class U2): Any projection of the fundus in the midline, equal to or more than one third distance from the internal os to the fundus, can directly be called a septate uterus (fig 2). Smaller indentations than this may be arcuate rather than septate. This is however, a subjective assessment and not nearly as reliable as measuring the depth of the septum in relation to the myometrial thickness on 3D USG, which is considered the gold standard.

There is no universally accepted technique of making objective measurements inside the uterine cavity. The graduated uterine palpator by Karl Storz is used at some centres [6]. The other way to get an approximate estimate of distance is using a hysteroscopic instrument (grasper or scissor).

The distance between the open jaws of the instrument is first measured outside the uterine cavity. Using this information, the total length of the septum is assessed during surgery without actually cutting the septum. Similar information can also be obtained by using the straight resectoscope loop [7].

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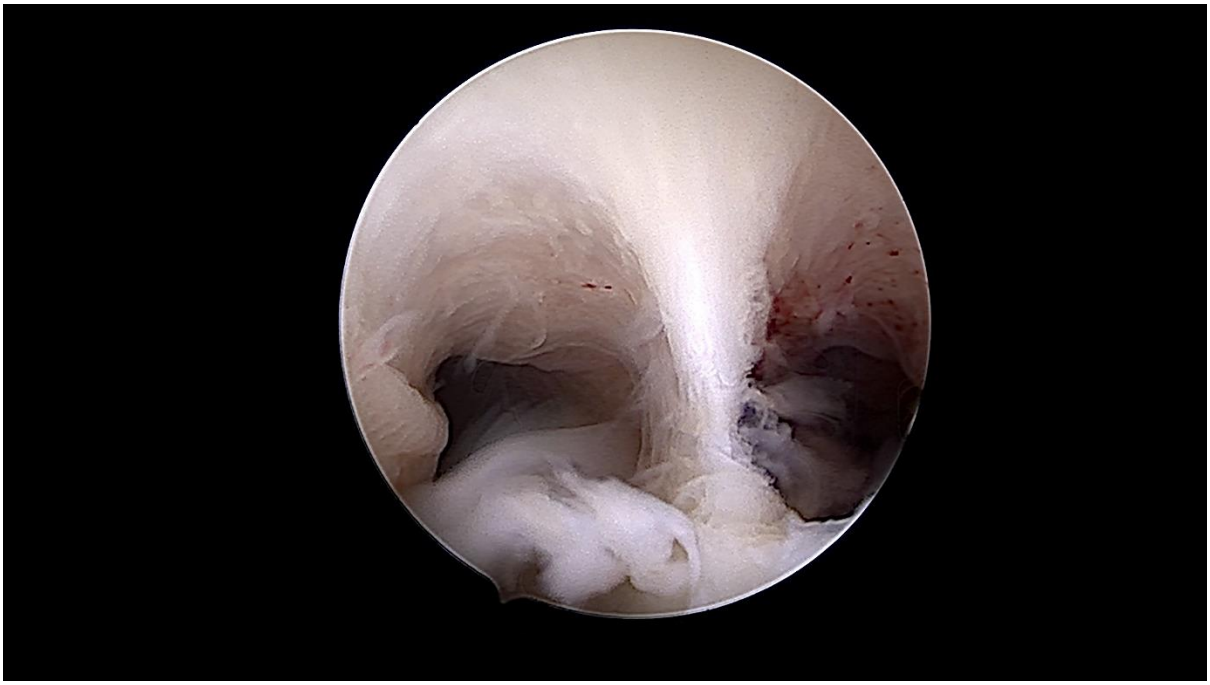

Figure 1. Septate uterus (U2a). By S. Pisat.

There is consistent data indicating arcuate uterus as an acceptable variety of normal uterus, which does not need any surgical repair.

b. The T shaped uterus (Class U1): a tubular, tunnel like cavity is seen beyond the internal os. Both tubal ostia are not visualised (fig 3). The telescope has to be advanced higher into the uterine cavity, usually beyond half the distance of the cavity. At this stage, tilting the light cable allows visualisation of the tubal ostium. In case of a unilaterally convergent wall (the 7 shaped uterus), the view of only one of the ostia may be hindered by the hypertrophied lateral wall, and the other ostium clearly seen from the internal os. Making this observation carefully at this stage is very important, because this is also considered as the end point of surgical correction once the lateral wall has been incised with an electrode or a scissor.

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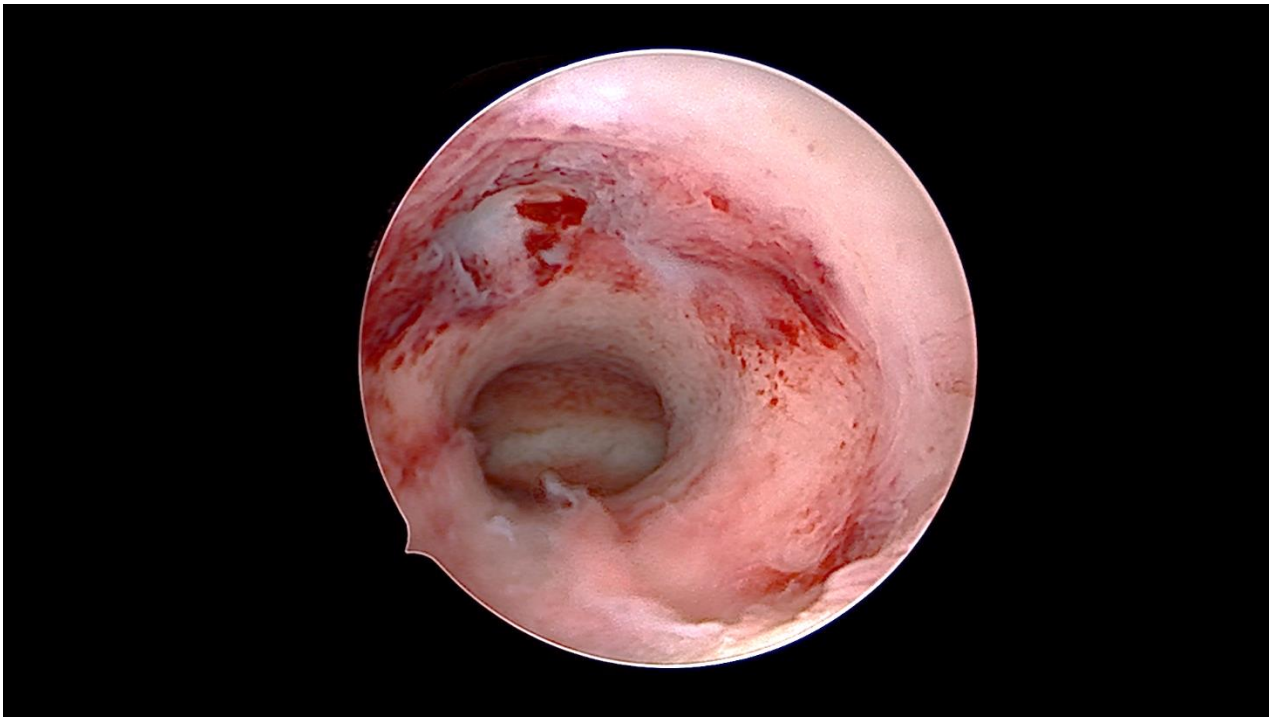

Figure 3. Narrow cavity of T shaped uterus (U1a). By S. Pisat.

It is worthwhile to remember that a uterus which is hypoplastic may have a cavity that looks exactly like that of a T shaped uterus which is normal in size externally. The distinction between these two must be made on pre operative imaging by 3D ultrasound, because only the latter is a case justified to undergo surgical correction

c. The bicornuate uterus (Class U3): The cavity of a bicornuate unicollis uterus looks exactly same as that of a completely septate uterus. It is very important to distinguish between the two, because a casual septal incision initiated by just seeing an inward midline indentation could result in a catastrophic perforation if the uterus is bicornuate, or bicorporeal septate, rather than septate. This distinction can be made pre operatively using a 3D ultrasound to define the degree of serosal indentation, or intra operatively by performing a concomitant diagnostic laparoscopy

d. The unicornuate uterus (Class U4): a banana shaped, rather than a tubular cavity is seen with a single terminal ostium. Obviously, the volume of the cavity is reduced. The surgeon must be careful to make sure that he/she has not missed the other half of a bicornuate uterus, and mistakenly visualised only one half of the cavity thereby labelling it as a unicornuate uterus. It is best to confirm the size and functionality of the other horn by

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performing a simultaneous diagnostic laparoscopy

e. The Accessory cavitated uterine mass (ACUM) (Class U6): Previously known as juvenile cystic adenoma (JCA), ultrasound leaves behind a diagnostic dilemma, confusing the entity with a functional non communicating uterine horn with hematometra. In both cases, the patient presents with severe dysmenorrhoea. In these cases, a diagnostic hysteroscopy performed before laparoscopy effectively rules out the possibility of a non-communicating horn, if both ostia are visualised.

f. The Robert's Uterus (Class U6): this condition is also best diagnosed by pre operative pelvic MRI, and is an asymmetric fusion of the vaginal septum to one side of the midline. Consequently, hematocolpos and hematometra, sometimes hematosalpinx ensues. On vaginoscopy, a bulge is seen distending one half of the vagina, and only half the circumference of the cervix is visible. The appearance of the uterine cavity, before corrective surgery is performed, is like a unicornuate uterus [8].

Conclusion

In summary, diagnostic hysteroscopy plays a vital role in both the diagnosis and management of congenital anomalies of the genital tract. Used in conjunction with clinical examination and imaging, hysteroscopy provides an invaluable tool for assessing and correcting these anomalies resulting in optimal surgical outcome.

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Isthmocele: new insights and review.

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Abstract

Isthmocele is an anatomo clinical entity still lacking standardization in its diagnostic and therapeutic approaches. It is a condition where building bridges between ultrasound and hysteroscopy is particularly fruitful. The surgical management of the symptomatic forms can be conducted through hysteroscopic, laparoscopic, vaginal or laparotomic routes. In this article is provided a review of the relevant data of the literature exclusively related to its diagnostic aspects. An overview of the main hysteroscopic and sonographic findings encountered in practice is also discussed and provide new insights on the condition's pathogenesis. Although the niche has long been thought of as a static defect causing accumulation of menstrual blood, it is also likely to act as an active valve closing the internal ostium of the cervix and causing fluid dynamic changes as described by an Indian team. Additional observations during hysteroscopy allow collecting different anomalies which are likely to explain the usually encountered symptoms such as abnormal uterine bleeding, subfertility, chronic pelvic pain, dysmenorrhea and dyspareunia.

Key words: cesarean scar defect, complex isthmocele, inflammation; vascular changes; endometriosis, dynamic changes.

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Introduction:

The isthmus is the lower uterine segment (LUS) lined by a poorly hormone-responsive endometrial mucosa, whose anatomic lower limit is the histological internal os of the uterus (commonly termed internal os of the cervix) and whose anatomic upper limit is the anatomical internal os of the uterus, first described in hysteroscopy in 2020 (1).

Isthmocele etymologically means hernia of the isthmus and by extension, it is the defect resulting from an impaired healing of both the endometrium and myometrium at the site of the cesarean incision. It is also termed cesarean scar defect (CSD), niche, pouch or diverticulum and was first described in these terms in 1995 by Hugh Morris on hysterectomy samples of women who suffered of persistent abnormal uterine bleeding (AUB) without any other identifiable condition (2).

The prevalence of isthmocele ranges from 24% to 70% in transvaginal ultrasound (TVUS) examination according to some authors, although the exact number is unknown and difficult to assess (3). The risk factors so far associated with the genesis of a CSD are summarized in table 1 (4-6).

Many patients may be asymptomatic, yet in premenopausal women, post menstrual AUB is the most classic symptom with a variable impact on patients' quality of life. Chronic pelvic pain, secondary subfertility, dysmenorrhea and dyspareunia are among the well-established consequences of this condition, let alone the potential obstetrical complications during an upcoming pregnancy such as scar pregnancy, placenta accreta and scar dehiscence (3,4,7).

In the persistent lack of high quality evidence and standardization of isthmocoeles diagnosis and treatment (8), this article aims to review the relevant data of the literature which are exclusively related to the condition's diagnostic and etiopathogenic aspects, with a special focus on the hysteroscopic and sonographic findings encountered in practice and which provide additional insights on the pathogenesis of the commonly encountered symptoms, namely AUB, subfertility, chronic pelvic pain, dysmenorrhea and dyspareunia.

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Risk factors of isthmocele	Specificities	Comments
Surgery-Related Factors	Cervical location of the uterine incision	Local mucus secretion causing poor healing and distension of pouch
	Incomplete closure of the uterine wall	Defects in the involved sites
	Single layer uterine closure	A longtime unresolved debate preferably requiring randomized control trials (RCTs), to which the latest systematic review revealed inferiority of single layer closure (5)
	Locked sutures as opposed to non locking ones	Increased tissue hypoxia and subsequent poor healing
	Post operative infection of the uterine scar.	Tissue devascularization, ischemia causing poor healing.
Patient-Related Factors	Individual differences in wound healing	Due to individual varieties of immune response and healing process
	Gestational diabetes and obesity	Known to impair inflammation
	number of previously performed C-section	According to a study, 100% of patients with a histoty of 3 cesarean section were prospectively diagnosed with isthmocele
	Cesarean sections performed in the second stage of the labor	Mostly performed on the cervix
	Uterine position	Higher prevalence in retroflexed uteri than in anteflexed ones

Table 1. Main risk factors associated with isthmocele.

Simple isthmocele: a triangular defect collecting menstrual blood.

Posing the diagnosis of isthmocele starts with a two-dimensional (2D) ultrasound for the visualization of the defect, its length from up to down, its 2 mm minimum depth as well as the residual myometrium (9). It is located inside the cervix, the isthmus or the cervico-isthmic level. Three-dimensional (3D) ultrasound additionally provides the lateral width of the pouch and in case of difficulties; saline/gel infusion

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sonography allows clearer visualization through distension.

At the thought of the term isthmocele, the ultrasonographic image of a triangular anechoic area in the LUS comes to mind, as well as the thought of a pouch where menstrual bleeding is cyclically collected –due to reduced uterine contractility by to the presence of scar tissue– and subsequently released in the form of blackish or brownish spotting. This triangular shape is limited by a distal edge oriented towards the cervix; a proximal edge closer to the uterine corpus and a roof, on top of which lies the residual myometrium separating the defect from the serosa (10) (Fig 1).

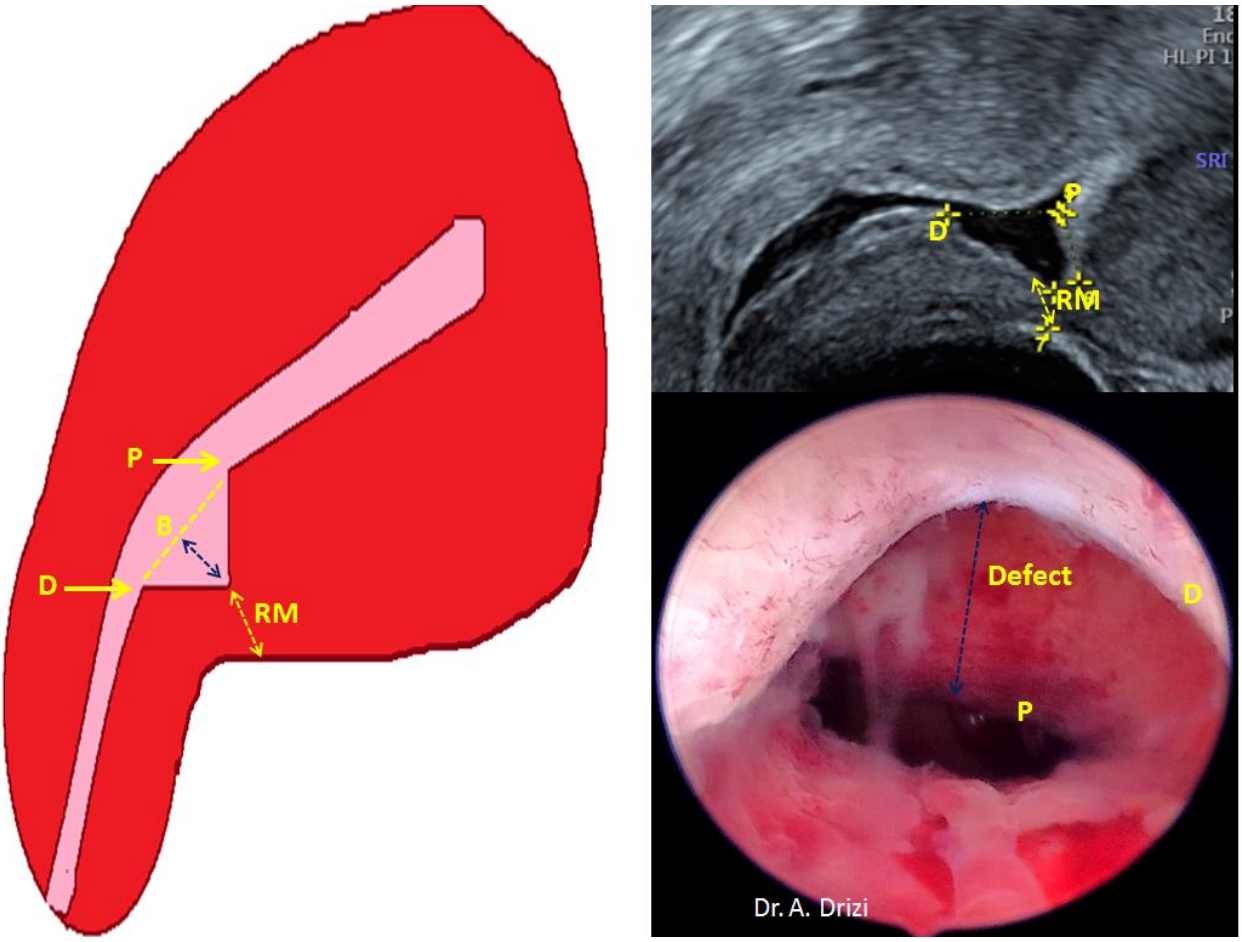

Figure 1. Correlations between 2D ultrasound of isthmocele and diagnostic hysteroscopy. D: distal edge; P: proximal edge; B: basis; blue arrow: depth of the niche; RM: residual myometrium. Images by A. Drizi.

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The distention of the CSD by blood could be such that it mimics the uterine cavity when hysteroscopy is performed by a non-warned practitioner. This highlights the importance of proper irrigation and evacuation of blood during hysteroscopy, with a gentle progression of the scope and particular attention to the anatomical landmarks defining the uterine cavity, mainly the tubal ostia.

The persistence of menstrual blood in the cervico-isthmic level is described to negatively influence mucus quality as well as the environment for sperm transport and embryo implantation, also acting as a physical barrier in embryo transfer during assisted reproduction technologies (ART), secondarily causing infertility (8). However, there is lack of high-quality data regarding these mechanisms.

The hysteroscopic management of isthmocele exclusively targets this particular simple triangular pouch with a minimum residual myometrium of 2.5-3 mm and consists of coagulating its roof after resection of either the distal edge alone in Fabre's technique (8, 11); the distal and proximal edge in Gubbini's classic technique 2008 (10) or channel-like 360° resection of the whole canal in the latest proposed techniques (12) (Fig 2). Resection of the hard fibrous tissue is thought to allow subsequent remodeling of the residual myometrium under improved uterine contractility. However, to date there is no comparative study to prove the superiority of any technique over the other.

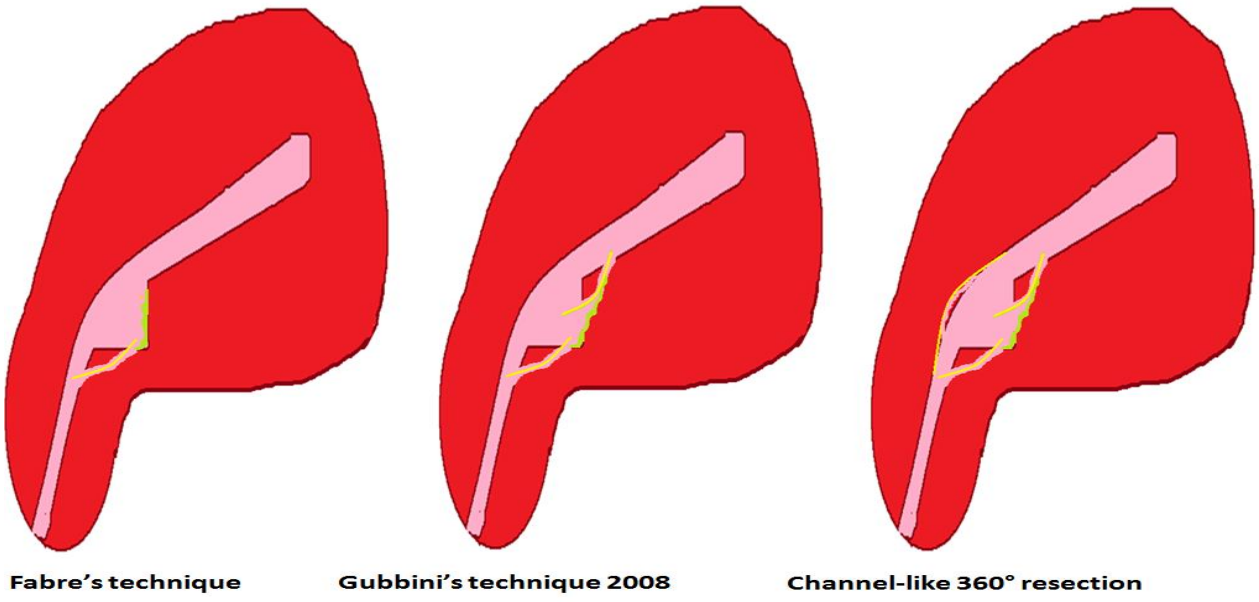

Figure 2. The hysteroscopic techniques of isthmocele treatment.

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More importantly, this simple triangle-shaped isthmocele only addresses the simplest form of CSD which, time passing, reveals various shapes and complex mechanisms needing to be acknowledged and addressed in the surgical treatment.

Complex isthmocele: atypical anatomy – heterogeneous shapes and branching

One of the problems resulting from the absence of pertinent consensual definitions of isthmocele is experienced when dealing with cases of CSD which are different from the above-mentioned simple triangle-shaped ones.

In fact, all practitioners usually encounter morphological differences in real life practice. Ultrasonography experts have already proposed a more consistent classification taking into consideration the heterogeneous shapes and branches of the USDs, which do not always happen to be wedge-shaped but at times mimicking a round, square or even a cribriform area (8,9,13).

The presence of branches in the roof of the isthmocele is particularly important to note as it classifies the CSD among the complex ones and as it decreases the real residual myometrium which always needs to be measured at the site where it is the thinnest (9, 13) (Fig 3).

The presence of Nabothian cysts at the level of the uterine scar is another common anatomical finding which can be misleading to over-diagnosis of CSD whereas it is a differential diagnosis (8) (fig 3)

However, whether the USD is anatomically complex and/or associated with Nabothian cysts, its hysteroscopic management remains unclear as there are to dates no guidelines to specify how to approach them.

The presence of branches has already been acknowledged by the ultrasonographers as modifying the level at which the residual myometrium needs to be measured: rather from the top of the branch and not from the roof of the niche itself (9, 13). During diagnostic hysteroscopy, attention should be given to the movement of air bubbles within the niche, as they tend to go through the branches' orifices (fig 3).

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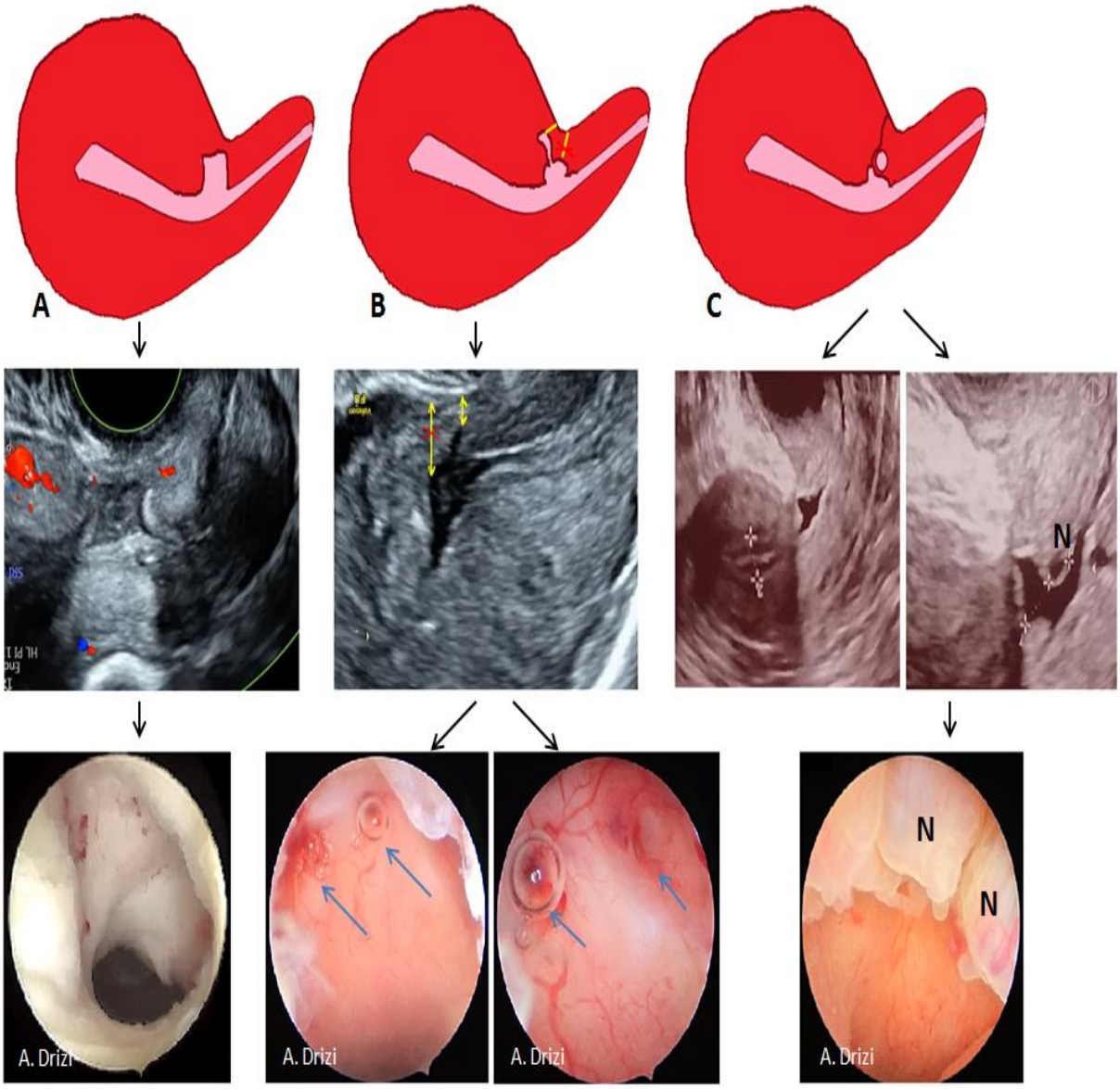

Figure 3. Complex anatomy of isthmocele with sonographic and hysteroscopic correlations. A: square-shaped niche; B: branch on the top of the niche with air bubbles passage at hysteroscopy through the orifices; C: Nabothian cyst near isthmocele. Yellow arrow: residual myometrium; Blue arrow: the orifice on the top of the niche leading to the branch with air bubbles passage (complex isthmocele). N: Nabothian cyst. Images by A. Drizi.

Still, the question of how to optimally resect an anatomically complex isthmocele via hysteroscopy has never been addressed in a study. Moreover, the anatomical varieties of operated niches are never detailed in the available studies.

And just as importantly, the complexity of CSD is not only anatomical but seems to involve additional non anatomical mechanisms which requiring closer attention.

Complex mechanisms in isthmocele other than blood collection: vascular, inflammatory,

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polypoid, endometriotic and myometrial changes.

In addition to the classical pathogenic mechanism of menstrual blood trapped in and distending the CSD, in-situ provenance of the bleeding has already been mentioned by some authors.

Among the etiopathogenic factors of isthmocele, cervical location explains local mucus-like secretion thus perturbing the healing process and causing local inflammation (4). The latter is well known to cause AUB, also because of the resulting abnormal vascularization around the scar (10).

Chronic inflammation is already known for being the optimal ground for proliferative processes in all branches of medicine. Its role as a risk factor for the development of endometrial polyps has already been documented in the literature (14). Although its association with symptomatic isthmocele has never been assessed to date, polyps are not a rare finding in our practice. In-situ bleeding from abnormal local vessels of the niche is not rarely encountered in our practice either (Fig 4).

In addition to inflammatory, polypoid and vascular anomalies, endometriosis has also been reported as a non-negligible intraoperative finding in patients with symptomatic isthmocele, with a special focus on the laparoscopic approach, especially in women with secondary infertility and dysmenorrhea (15,16). Isthmocele is thus a recent condition still requiring more investigations.

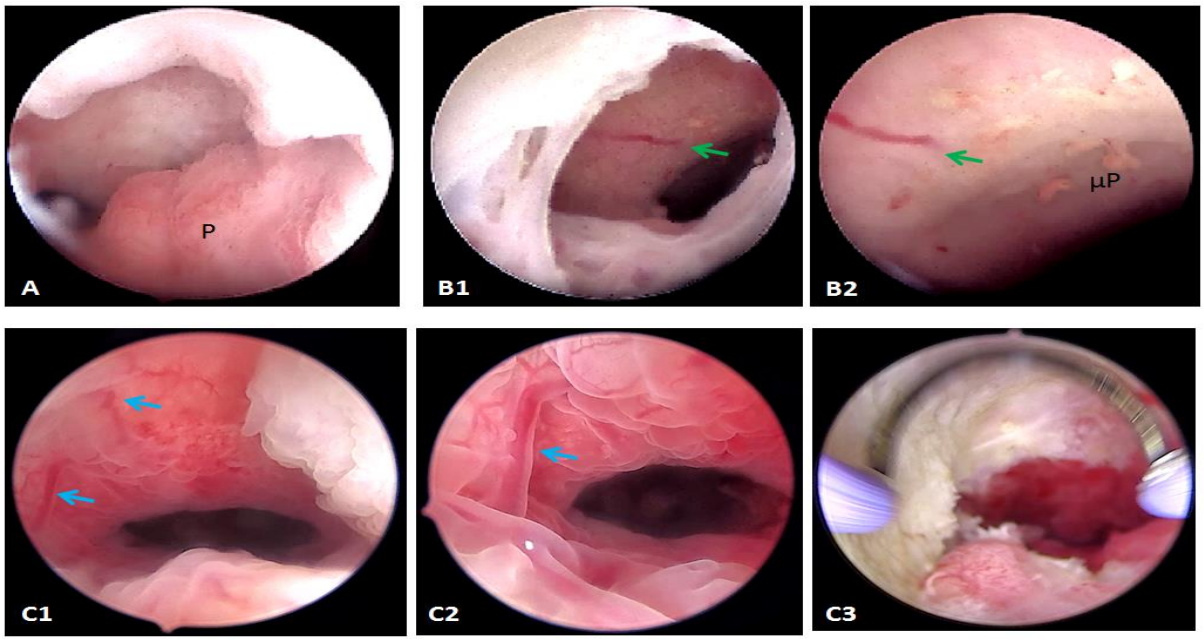

Figure 4. Complex mechanisms involved in the isthmocele's pathogenesis. A: Polyp (P) inside the niche; B1: Spontaneous bleeding from a vessel on the roof of the niche (green arrow); B2: closer view with inflammatory patterns like micropolyps (µP); C1: ectatic vessels in a symptomatic niche (Blue arrows); C2: Closer view; C3: after resection and coagulation. Images by A. Drizi.

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Myometrial changes could be thought of as the resulting altered muscular contractility due to the presence of a hard fibrous scar tissue within an elastic dynamic muscle, hence perturbing its contractility. This has been described as one of the factors causing abnormal evacuation of menstrual blood outside the uterus during menses (10). Regardless of that, isthmocele being considered as a static distended hernia passively collecting blood can also be questioned, especially as the uterus is a muscular dynamic organ.

Complex isthmocele: a dynamic entity? The Aggarwal valve.

In all the available published data on isthmocele, the defect is always presented as a distended static space where secretions and blood can be collected and subsequently released in the form of post menstrual bloody discharge. The only dynamic facet of CSD is the myometrial contractility which is reportedly altered by the presence of scar tissue.

However, an Indian author has recently reported cases where the distal edge of the niche is acting like a valve under myometrial contractility thus closing the cervical canal and explaining cryptomenorrhea. This is explained by the enlargement of the pouch and the consequent thinning of the wall both towards serosa and cervical canal which would result in a distal edge taking the form of a fibrous-mucosal fold oriented towards the canal and which, just like a valve, would close the passage to the canal when pushed down by the blood flow, thus decreasing evacuation of menses (17) (fig 5).

This dynamic pathogenic mechanism is indeed observed at ultrasound in some cases where the movement of the distal edge of isthmocele is filmed during uterine contractions (Fig 5). In hysteroscopy, it is difficult to observe this phenomenon as the distending medium movement goes from the cervix to the cavity in order to open the virtual spaces.

Therefore, although laparoscopic resection was the technique demonstrated for this mechanism, it appears that hysteroscopic resection is also effective as all the usual techniques (10-12) target the distal edge of the niche, hence allowing suppression of the valve-like acting system. Of course, more studies are needed to explore in depth this potentially path-breaking dynamic mechanism.

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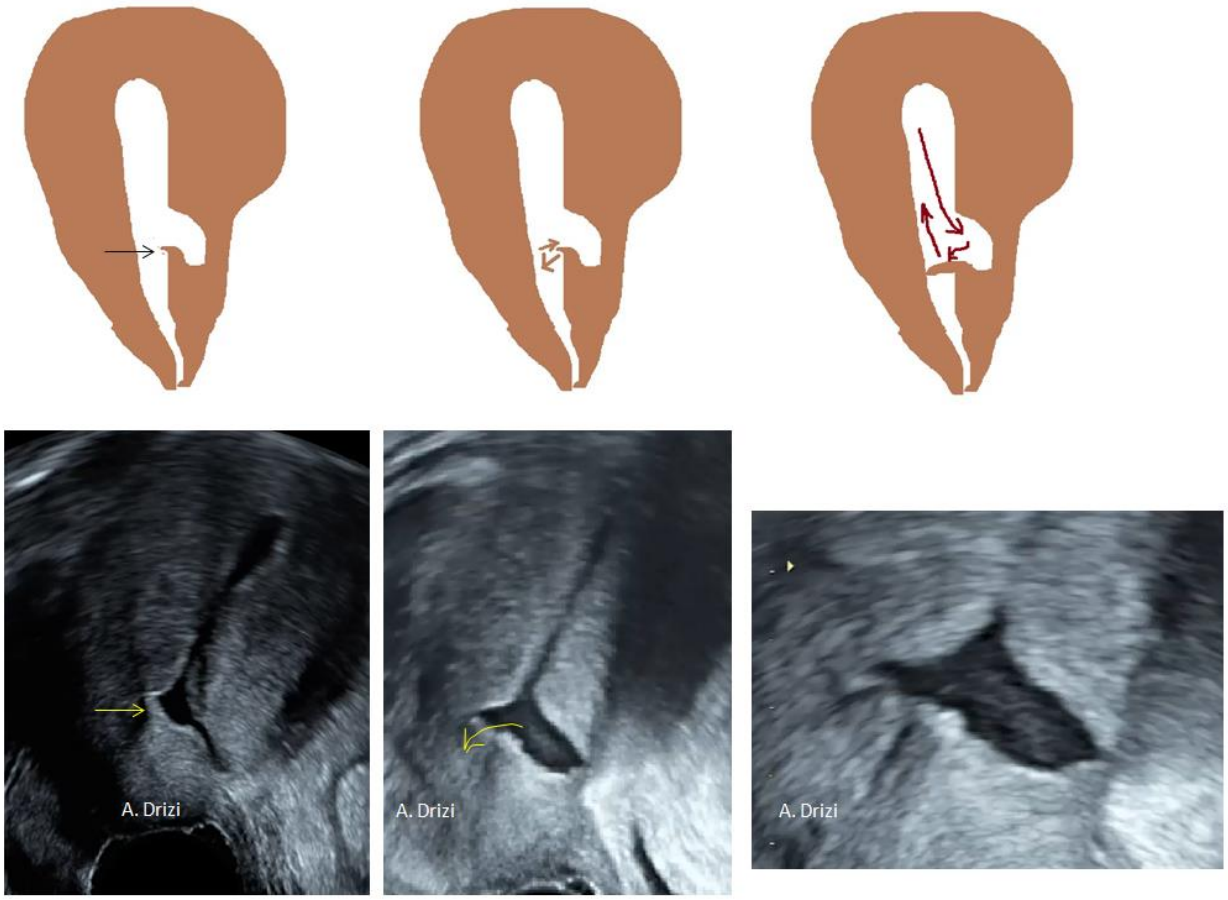

Figure 5. Demonstration of the valve mechanism by the distal edge and correlation with ultrasound at increasing magnification (black and yellow arrows). The flow of the blood closes the valve resulting in decreased evacuation of menses and causing more distention. Images by A. Drizi.

Isthmocele: rather a complex multifactorial entity.

Given the lack of standard consensus regarding classification and management of isthmocele, it is of utmost importance to remain careful to the various mechanisms in order to identify this or those involved in each patient, so as to thoughtfully target them whenever possible. Moreover, reporting the diagnostic details of the operated cases is the only warrant of more pertinent studies leading to a better understanding of the condition in its diverse facets as well as to more optimized treatment strategies depending on the variety's type. Consequently, a constant attention to details during diagnostic hysteroscopy is of high importance, as it can reveal additional anomalies which are difficult to judge at ultrasound such as angulations and twisted path of the cervico-isthmic canal (Fig 6).

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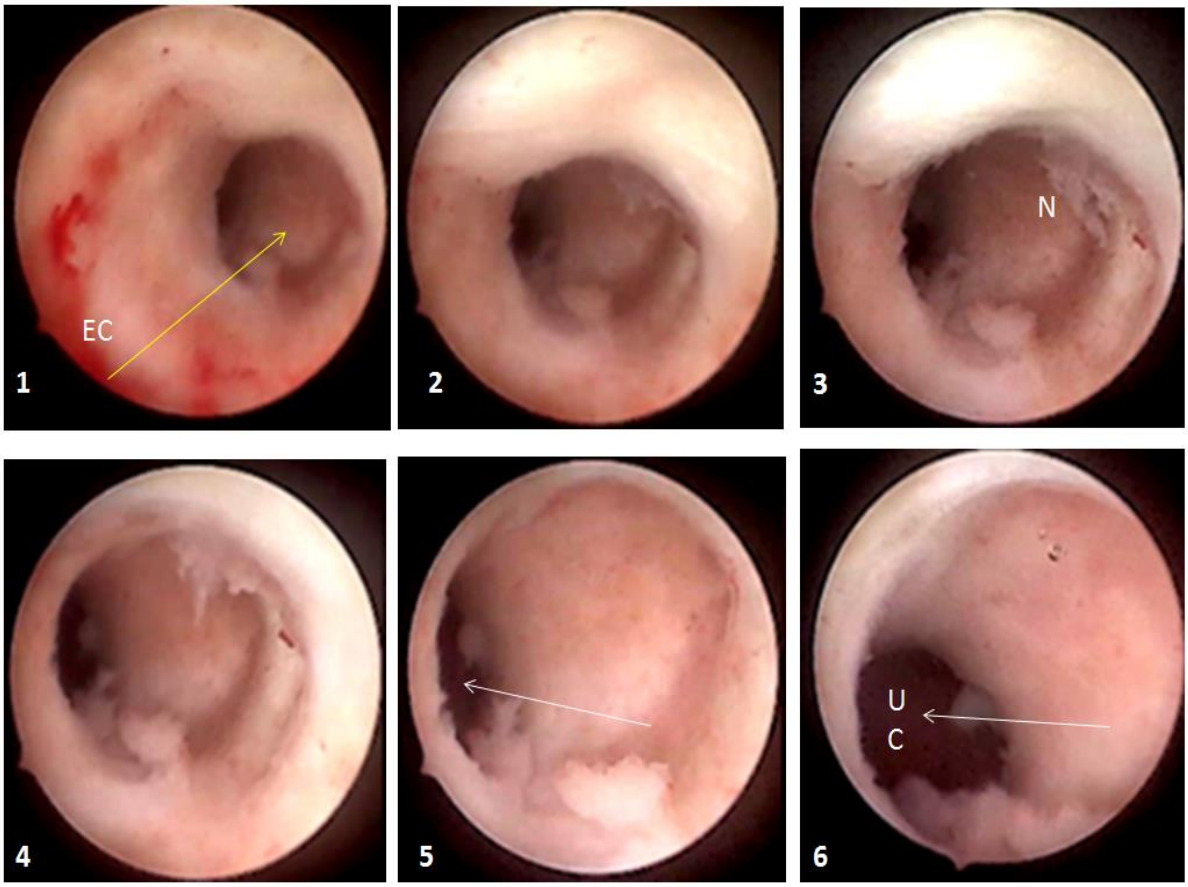

Figure 6. Lateral angulation at the level of the niche (N). 1-6: progression from the endocervical canal (EC) until the entry of the uterine cavity (UC). Yellow arrow: orientation of the canal from the right to the left of the patient; white arrow: orientation of the cavity from the left to the right of the patient, resulting in an angulation (images by A. Drizi).

In table 2, a diagram is proposed to summarize the different classes of isthmocele overviewed in this article, as well as the therapeutic approach likely to tackle the specific pathogenic mechanism in each one.

Conclusion

With the progress of imaging techniques, hysteroscopy does not need to be performed in the unique purpose of posing the diagnosis of a symptomatic isthmocele but rather as a mandatory first step within the same operative session.

DOI: 10.36205/trocar1.2023013

Pathogenic mechanisms of isthmocele	Specificities of the symptomatic defect	Proposed surgical adaptation in hysteroscopy.
Anatomical varieties	Simple triangular USD • RM greater or equals 2.5-3mm • RM < 2.5mm Complex shapes Complex USD with branches	Classic hysteroscopic treatment Laparoscopy, vaginal route Depending on the RM Laparoscopy++, vaginal route++ If RM > 3mm: hysteroscopic opening of the branches to be assessed?
Histo-pathological varieties	Vascular anomalies Inflammation Polyps Endometriosis Adenomyosis on the roof Myometrial changes.	Coagulations of all abnormal vessels Release of the distal edge to facilitate evacuation of blood + coagulation of all the inflammatory tissues Polypectomy Superiority of laparoscopic or vaginal resection of the entire wall. Coagulation (⇔cautery) Hysteroscopic resection of the hard fibrous tissue allows subsequent remodeling of the myometrium within the scar site.
Dynamic varieties	Distal edge acting as a valve-like system	Hysteroscopic resection of the distal edge (plus the usual hysteroscopic treatment).

Table 2. Summary of the different classes of isthmocele overviewed in this article, as well as the therapeutic approach likely to tackle the specific pathogenic mechanism in each case.

Despite the lack of understanding surrounding the isthmocele as an anatomo-clinical entity, it appears as a multifactorial condition where heterogeneous mechanisms can be impaired.

Its appears as one area where ultrasonography and diagnostic hysteroscopy are more advanced than operative hysteroscopy which, in all cases,

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can only be improved if taking into consideration the different varieties.

It is of utmost importance to define more pertinent classifications of the condition separating the simple classic forms from the complex ones as this could impact the choice for the optimal surgical treatment. Therefore, and in our practice of ultrasound and diagnostic hysteroscopy, we propose to classify isthmoceles in simple and complex ones. Complexity can be anatomical, histo-pathological and dynamic. This would provide a more accurate basis for the assessment of the surgical treatment.

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Diagnostic hysteroscopy: complications, Diagnosis and management.

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Abstract

Diagnostic hysteroscopy is associated with less complications as compared to operative hysteroscopy, but one should remain vigilant about any complications that may occur as it may be lethal. The main purpose of this paper is to summarize the complications of diagnostic hysteroscopy and its diagnosis, the necessary preventive measures and management according to the available papers through a non-systematic review of the literature.

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Outcome: Perforation being most common complication of diagnostic hysteroscopy can be managed either conservatively or laparoscopically. The other serious complications such as fluid overload, electrolyte imbalance and air embolism may be associated with the diagnostic hysteroscopy.

Conclusion: The gynecologists should be alert in order to assess, prevent and manage various complications associated with diagnostic hysteroscopy. The focus should be on proper patient selection, appropriate surgical technique and good instruments, so that the complications could be avoided.

Key words:

Diagnostic hysteroscopy; complications; uterine perforation; false passage; air embolism; management.

Introduction

Diagnostic hysteroscopy is considered to be a safe procedure as it is associated with minimal complications. Hysteroscopy is gaining popularity amongst the gynecologists as a diagnostic and therapeutic tool for various gynecological pathologies such as polyps, myoma, intrauterine adhesions (IUA), uterine anomaly, infertility and cervical pathology etc. It is very important to prevent, recognize and appropriately manage complications associated with hysteroscopy. Disregarding contraindications and/or the appropriate technique of the procedure can lead to complications in hysteroscopy.

The main purpose of this non-systematic review of the literature is to summarize the complications of diagnostic hysteroscopy as well as its diagnosis and management according to the available data.

Various complications associated with diagnostic hysteroscopy

Diagnostic hysteroscopy is a relatively safe and well-tolerated procedure as compared to any other invasive gynecological procedure. Following are the rare complications associated with the procedure and if left unnoticed can become lethal (figure 1). Hence one should be vigilant and efficient enough to prevent them or if in case it occurs recognize them immediately and manage accordingly.

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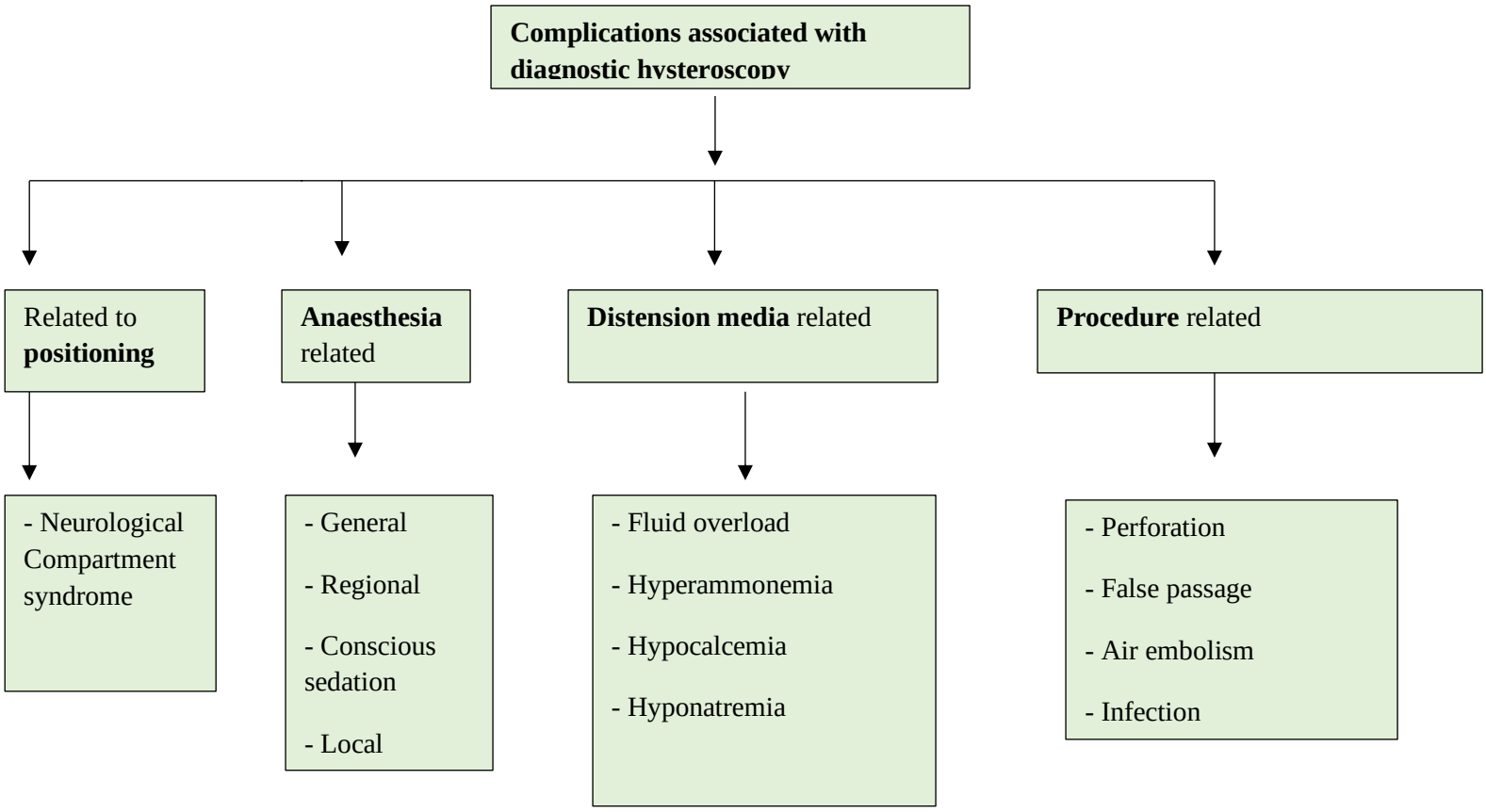

Figure 1. Schematic representation of various complications associated with diagnostic hysteroscopy.

The most common complication associated with both diagnostic and operative hysteroscopy is uterine perforation (1,2). Figure 2 depicts uterine perforation during hysteroscopic procedure and its management on laparoscopy.

Figure 2. Iatrogenic uterine perforation due to hysteroscopy and its laparoscopic management.

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The general condition of the patient, cause, location, bleeding and severity of the uterine perforation are the basis of management of uterine perforation. It is important to note that at every step of hysteroscopy like dilatation of cervix, sounding of the uterus, the placement of hysteroscope, or the use of instruments for specimen removal, may lead to defect in the uterine myometrium. In cases where the uterine entry is difficult due to stenosis, nulliparous or menopausal cervix there are chances of formation of false passage during hysteroscopy as depicted in figure 3 but insufficient data is available on false passage creation till date due to underreporting.

In a recent study, the use of misoprostol for pre-procedure ripening of cervix showed decreased incidence of false passage creation but uterine perforation rates were not reduced (3). Immediate surgical intervention is needed in case of perforation by an electrosurgical electrode, heavy bleeding or suspected visceral injury (fig 2). The scheme for diagnosis, management and various risk factors of uterine perforation due to hysteroscopy are listed in figure 4.

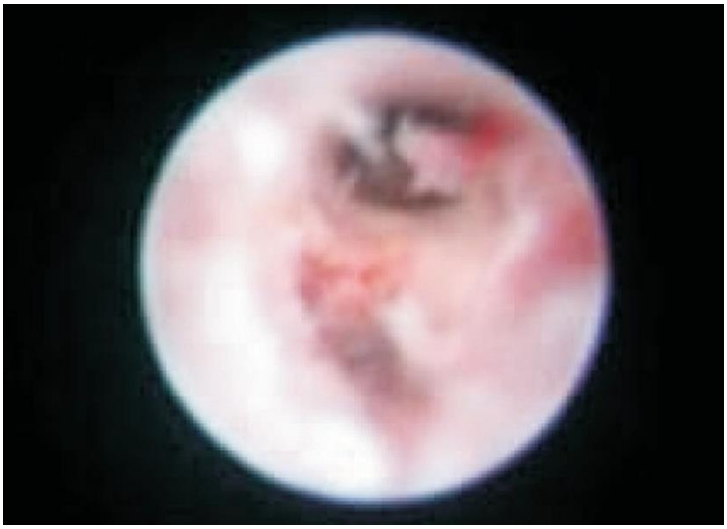

Figure 3. False passage located posteriorly to the internal cervical os.

Infection:

For routine hysteroscopic procedures use of antibiotics as a prophylaxis is not recommended. In women with active pelvic infection or herpes infection hysteroscopy is contraindicated[5]. The incidence of infections like endometritis and urinary tract infections as a postprocedural complication of hysteroscopy is rare which ranges from 0.01% to 1.42% (1, 6).

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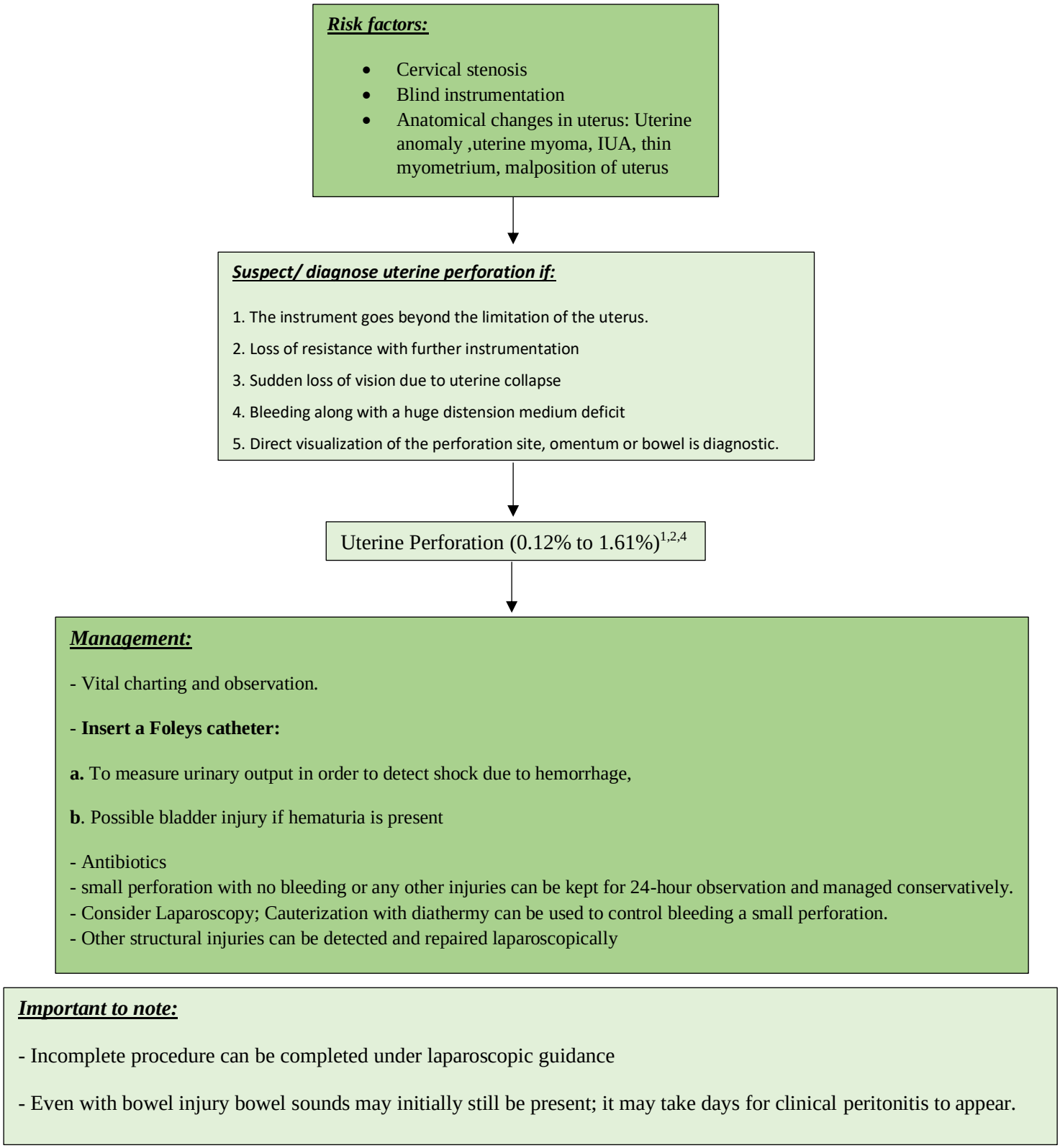

Figure 4. Scheme for diagnosis and management of uterine perforation.

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In various studies, in both diagnostic and operative hysteroscopy the antibiotic prophylaxis coverage has not found to decrease the incidence of post procedural infection (7,8,9). In a study conducted on 1,952 cases with operative hysteroscopies, the higher risk of endometritis was found after adhesiolysis as compared to myomectomy or polypectomy (10).

Fluid Overload

In some rare cases lethal complications such as neurologic complications, pulmonary edema and even death may occur due to excessive distension media absorption.

There is an increased risk of hypotonic hyponatremia and cerebral edema associated with the use of hypotonic, electrolyte-free distension media. With the proper pre-operative assessment of the intrauterine lesions, vigilant prior planning and use of a hysteromat to measure fluid deficit one can minimize these complications associated with fluid overload.

Fluid deficit is observed mostly with operative as compared to diagnostic hysteroscopy affected by intra uterine pressure kept during procedure, duration of the procedure, number and size of the pathologies removed, the number of myometrial sinuses opened, and the depth of myometrial resection.

It can be prevented by limiting excessive fluid absorption, early and prompt recognition and management of fluid overload, and selecting a distending medium that minimizes risks. Intravasation of fluid can be reduced by injecting Vasopressin in the cervical stroma (11). A close and frequent monitoring of the fluid deficit during the hysteroscopy is the best way to limit excess fluid intravasation. Fluid overload is firstly managed by termination of hysteroscopic procedure; followed by evaluation of hemodynamic, respiratory, cardiovascular and neurologic status; osmolality and serum electrolytes are to be checked; and diuretic administration may be considered. Nowadays fluid monitoring has become easy and precise with the newer fluid management systems like hysteromat; however, these are not readily available in all settings due to their high cost.

Fluid Monitoring guidelines and the measures to limit fluid excess (12)**:**

1. Close monitoring of intravenous hydration of patients during both preoperative and intraoperative period.
2. Close watch on intra operative hysteroscopic fluid absorption.
3. For old aged patients, or having associated comorbidity, having cardiovascular or kidney dysfunction, and in an outpatient setting lower fluid deficit thresholds should be considered.

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4. The upper limit of fluid deficit in healthy patients is 2,500 mL for isotonic fluids, 1,000 mL for hypotonic fluids, and 500 mL for high-viscosity fluids. But, if fluid deficit reaches 2,000 mL of isotonic fluid, 750 mL of a hypotonic fluid, or 300 mL of a high-viscosity fluid, further infusion should be stopped and finish hysteroscopy. Anesthetist must be involved in such decision and further management, if applicable.
5. Fluid deficit threshold is further lowered in an outpatient setting due to limitation of quick care and laboratory facilities.
6. Early recognition of fluid deficit in real-time can be best measured by an automated fluid monitoring system.
7. A person should be made in charge to evaluate intake and outflow of the fluid frequently and inform the fluid deficit to the surgical team.
8. If maximum fluid deficit occurs general condition and systemic assessment apart from signs and symptoms of fluid overload should be done. Thorough evaluation of osmolality and serum electrolytes is done, diuretics given, and other measures taken as indicated. Further treatment of fluid overload or hyponatremia may need corrective fluid infusion, multidisciplinary team management in a critical care setting.

Air and Gas Embolism

The use of carbon dioxide (CO2) as a hysteroscopic distension medium may lead to air embolism as a complication in hysteroscopy, various risk factors include room air entering during cervical instrumentation or dilatation, Trendelenburg position or gaseous byproducts released during electrosurgery especially seen in operative hysteroscopy (13). As CO2 is more soluble in blood as compared to oxygen; so, greater risk of development of air embolism is associated with room air, which is a mixture of oxygen and nitrogen as compared to carbon dioxide (14). Cardiac or pulmonary failure or death are the lethal complications due to air or gas embolism. Dyspnea and chest pain are the usual symptoms associated with air or gas embolism, while if the patient is under anaesthesia then air embolism should be suspected with a decrease in end-tidal carbon dioxide (EtCO2) pressure or hypotension, tachycardia like hemodynamic changes are noted. The reported incidences of clinically significant gas embolism episodes associated with hysteroscopic procedure are very less in the literature (15,16).

Preventive measures for air or gas embolism include evacuation of air from hysteroscopic equipment and in flow tubing; restrict constant cervical insertion of instruments, which can push air in a “piston-like” manner in the uterine cavity and limiting intrauterine pressure. Minimize

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cervical trauma and if required, osmotic dilators may be considered preoperatively. Always keep the os closed so that room air entry inside uterus is avoided. Try to keep the previous dilator inside till hysteroscope or resectoscope is set up. Primary management of air and gas embolism consists of both conservative and active measures, like quick stoppage of the hysteroscopic procedure and uterine cavity deflation. Durant's maneuver, can be done to help in migrating air in the direction of right ventricle in order to decrease the obstruction at the right ventricular outflow tract, it can be performed by placing the woman in the Trendelenburg and left lateral decubitus position (14).

Vasovagal Reaction

The procedure should be stopped soon after identification of vasovagal features such as vomiting, diaphoresis, pallor, hypotension, bradycardia, nausea, or loss of consciousness and patient evaluation and conservative measures should be taken. Just by supportive measures like raising the patient's legs or placement in the Trendelenburg position will correct majority of the cases. Intravenous administration of atropine 0.5 mg every 3 to 5 minutes, up to 3 mg maximum is considered for treating bradycardia if present (17).

Intra-procedural and post-procedural pain may be reduced by 'vaginoscopic entry technique'. The efficacy of vaginoscopic approach is same as conventional entry technique[18].

Conclusion

Complications associated with diagnostic hysteroscopy are relatively rare and can be averted to a great extent with proper patient selection and pre-procedure evaluation, thorough technique and alertness for impending problems. Gynecologists must be aware about different types of distension media and specific enigma related with each in order to ensure the safety of the hysteroscopy. It should be made a priority for any consultant to understand the physiology and management of air embolism during hysteroscopy. In order to avoid any surgery related litigation clinicians must counsel the patients well regarding various complications and consequences associated with hysteroscopy and obtain a detailed consent before the procedure.

Main Points:

1. Proper patient selection, appropriate surgical technique and good instruments are to be checked always to prevent such complications.
2. A thorough knowledge of various distension medias and associated problems are must for safe surgery.

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3. Complications from fluid overload may be minimized with careful perioperative planning, use of a fluid management system.
4. The gynaecologists should be made aware about the pathophysiology and management of air embolism.
5. Small things like positioning also matters in this procedure.

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