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REVIEW

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Endometrial polyps

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Abstract

Endometrial polyps (EPs) are a frequent gynecological condition. EPs often arise in the common womanly patients and are appraised to be about 25%. Advancing age, hyperestrogenism, hypertension, and Tamoxifen use are acknowledged as ordinary risk elements for the development of EP. The etiopathogenesis of EP is not accurately elucidated, but certain considerations such as diabetes mellitus, hormonal factors or arterial hypertension are considered to perform a significant contribution. The diagnosis of EPs is essentially by imaging. Transvaginal ultrasound is the primary investigation in EPs. Hysteroscopic resection is now the "gold standard" to treat to treat this disease. Hysterectomy is the definitive treatment for EPs, but it requires a judicious indication and an adequate counseling of the patient. Currently, a certain histological pattern is found in different sequences in EPs. Even if the vast majority EPs are benign, they may reach hyperplastic, with malignant alteration. The purpose of this pictorial review is the integrated approach to this type of abnormal endometrial proliferation from the perspective of natural history, diagnosis, management, morphological aspects, risk of malignancy, recurrence and last but not least, clinical outcome.

Keywords: endometrium, proliferation, abnormal, diagnosis, morphology, histology.

Introduction

Uterine polyps are individualized endometrial protuberances which may arise all over, inside the uterine cavity. These structures encompass, in varying degrees stroma, glands and blood vessels, the proportional rates from each, revealing their hysteroscopic image [1].

Endometrial polyps (EPs) often arise in the common womanly patients and are appraised to be about 25% [2].

Symptomatic polyps typically cause abnormal uterine bleeding (AUB), the volume of this bleeding is usually reduced, meaning spotting in pre- and post-menopause, rarely manifesting as heavy intermenstrual bleeding, but they can constitute the background of significant menstrual blood loss [3].

Generally, EP are asymptomatic and are identified by periodic gynecological assessment or investigations accomplished in women addressing for infertility [2].

However, advancing age, hyperestrogenism, hypertension, and Tamoxifen use are acknowledged as ordinary risk elements for the development of EP [4].

Excepting the pedunculated polyps, prolapsed through the external cervical os, which appear as reddish friable globular formations, with a smooth surface, polyps do not cause other changes in the clinical examination [3, 5, 6].

EP can be solitary or numerous, averaging from some millimeters to centimeters, and can be pedunculated or sessile [7].

In terms of diagnosis, anyway, the customary availability of gynecological ultrasonography enables random EP diagnosis in asymptomatic patients [8].

Aim

In this pictorial review, we aim an integrated approach of EP, from a diagnostic, imaging, morphological and immunohistochemical point of view, in correlation with AUB and infertility.

Natural history and clinical approach

The specific risk of expressing EP rises from menarche to the end of the reproductive age [4, 9].

The etiopathogenesis of EP is not accurately elucidated, but certain considerations such as diabetes mellitus, hormonal

factors or arterial hypertension are considered to perform a significant contribution [2].

Recurrence is another defining feature of EP, especially under sustained Tamoxifen therapy [3, 10, 11]. Their natural history seems to be towards regression if the maximum diameter does not exceed 10 mm, in approximately 50% of cases, otherwise the tendency is towards growth and the appearance of new polyps [3].

Malpica *et al*. states that EP can be hyperplastic, atrophic, functional, mixed, and myomatous (Table 1) [12].

Table 1 – ***EP types***

EP type	Characteristics
Hyperplastic	Represents the most common form and is characterized by glandular proliferation, with variable shape and size, bordered by proliferative epithelium with mitotic activity; the interglandular stroma can be reduced, the differentiation from endometrial hyperplasia being made on account of the vessels with typically thickened walls and on the background endometrium's appearance, proliferative, atrophic or secretory.
Atrophic	Develop in postmenopause as endometrial structures with dilated cystic glands to a variable degree, delimited by cubical epithelium devoid of mitotic activity, separated by fibrous stroma.
Functional	Are responsive to hormonal stimuli, show proliferative changes or secretory underdeveloped compared to the surrounding endometrium; the stroma can be dense, edematous or predecidualized.
Mixed	Contain glands limited by an endometrioid or endocervical type epithelium, arranged in a usually fibrous stroma. Although it was initially considered to originate from the lower uterine segment, studies have demonstrated ubiquitous uterine implantation and frequent association with mucinous metaplasia common to the postmenopausal pattern.
Myomatous	Presents abundant smooth muscle tissue, along with glands surrounded by endometrial stroma, which makes it difficult to differentiate from adenomyomas. Squamous ciliated, mucinous or eosinophilic metaplasia is frequently associated with EPs.

Adapted from [3]. EP: Endometrial polyp.

For both pre- and postmenopausal women with an EP, AUB takes place in roughly 68% of patients and is the most usual presenting symptom for the cases with this condition [7]. Comprehensively discussing, 64% to 88% of premenopausal patients with EP have symptoms, almost all habitually presenting with irregular menses, menorrhagia, intermenstrual bleeding or postcoital bleeding [7, 13].

AUB and EP

The assessment and therapeutic conduct of AUB through nonpregnant patients in the fertile age phase was obstructed by the ambiguous or relatively inconstant carried-out terminology, as well as the absence of homogeneous means for exploration and organization of the different possible causes and factors [14].

Thus, the *International Federation of Gynecology and Obstetrics* (FIGO) approved an intuitive pattern, containing nine criteria that are defined conformably to the acronym PALM–COEIN (polyp, adenomyosis, leiomyoma, malignancy–coagulopathy, ovulatory dysfunction, endometrial, iatrogenic, and not-yet-classified) (Table 2) [14].

Table 2 – ***FIGO PALM–COEIN classification system [14–21]***

Pathological condition	Description	Acronym (FIGO)
Polyp	▪ Epithelial proliferations comprise an inconstant vascular, glandular, fibromuscular and connective tissue element; ▪ Usually benign; ▪ Often asymptomatic; ▪ A reduced minority may have atypical or malignant characteristics; ▪ Endometrial and endocervical polyps.	AUB-P
Adenomyosis	▪ US criteria for adenomyosis include the minimal demands to hypothesize in a patient the diagnosis of adenomyosis; ▪ US imaging of the internal endometriosis is in some measure connected to the essential existence of the ectopic endometrium within the myometrium; ▪ Distinction between diffuse and focal or multifocal types.	AUB-A
Leiomyoma	▪ Benign fibromuscular tumors of the myometrium; ▪ Subendometrial, intramural, subserosal, and combinations of these types; ▪ Many leiomyomas are asymptomatic.	AUB-L
Malignancy and hyperplasia	▪ Atypical hyperplasia and malignancy are considerable possible reasons of AUB; ▪ Have to be taken into account in almost all women of progenitive age; ▪ Relatively uncommon.	(AUB-M)
Coagulopathy	▪ This term includes the perspective of systemic abnormalities of hemostasis that can be related with AUB; ▪ Most often von Willebrand disorder.	(AUB-C)
Ovulatory dysfunction	▪ In some cases, results in HMB; ▪ Possible extreme HMB requiring medical or surgical intervention; ▪ May be linked to endocrinological disorders (hypothyroidism, hyperprolactinemia, Stein–Leventhal syndrome, obesity, weight loss, psychological stress, food aversion, or excessive training linked to performance athletics); ▪ Often happen in adolescence and climacteric translation; ▪ Certain occurrences bind to the lack of predictable cyclic progesterone secretion.	(AUB-O)
Endometrial	▪ Such anomalies can be subsidiary to endometrial infection and/or inflammation, disorders in the local inflammatory reaction, or errors in the endometrial vasculogenesis; ▪ HMB – can exist an initially disturbance of mechanisms controlling local endometrial hemostasis; ▪ Whenever AUB takes place in the circumstance of expected and periodic menstrual bleeding, characteristic to the ovulatory cycles, and especially when no other determinable reasons are recognized, the pattern is presumably an initial disruption of the endometrium; ▪ Imperfections in local secretion of vasoconstrictors like endothelin-1 and prostaglandin F2α, and/or expedited lysis of endometrial clot caused by the exaggerated production of plasminogen activator.	(AUB-E)

Pathological condition	Description	Acronym (FIGO)
Iatrogenic	▪ HMB represents a quite habitual reaction following the use of anticoagulant medication (low-molecular-weight heparin, heparin, warfarin); ▪ Systemically used sole or combined gonadal steroids, containing progestins, estrogens, and androgens influence the regulation of ovarian steroidogenesis through consequences on the hypothalamus–pituitary–ovary axis, and also achieve a straight impact on the endometrial tissue; ▪ Hormonal or passive intrauterine devices and pharmacological elements that directly interest the endometrial tissue, intercede with blood coagulation pathways, or affect the systemic command of ovulation; ▪ Systemic agents that intercede with dopamine metabolism have the potential to inflict AUB.	(AUB-I)
Not yet classified	▪ There may be other disorders, not yet identified; ▪ Various uterine pathologies could conduce to, or determine, AUB in a particular patient; ▪ Chronic endometritis, arteriovenous defects, and myometrial hypertrophy, have been weakly outlined and/or insufficiently considered.	(AUB-N)

AUB: Abnormal uterine bleeding; FIGO: *Fédération Internationale de Gynécologie et d'Obstétrique* (*International Federation of Gynecology and Obstetrics*); HMB: Heavy menstrual bleeding; PALM–COEIN: Polyp, adenomyosis, leiomyoma, malignancy–coagulopathy, ovulatory dysfunction, endometrial, iatrogenic, and not-yet-classified; US: Ultrasound.

Thus, according to this *FIGO* classification, Munro *et al*. consider the fact that patients presenting AUB can have none, one, or various recognizable elements that may concur to the occurrence of the anomalous bleeding [14]. Also, the same authors state that the examination of patients with AUB are required to be managed in as attentive and complete manner as is possible in the circumstances of the clinical condition and the existing equipment [14].

Overall, from the perspective of AUB, EP represent a very important segment of the PALM–COEIN classification, actually representing epithelial proliferations that include a varying vascular, glandular, fibromuscular, and connective tissue elements, usually benign and last but not least, the fact that a small but important minority may have atypical or malignant features.

Diagnosis of EP

The diagnosis of EP is essentially by imaging. Only in rare and random cases, especially in the conditions of AUB, they can be identified by pathology, in the conditions of a blind biopsy or in the absence of diagnostic resources.

Transvaginal ultrasound (TVUS) is the primary investigation in EP, especially in the presence of AUB or infertility.

On TVUS, an EP commonly shows up as a hyperechoic image with uniform outlines inside the uterine cavity, encircled by a fine hyperechoic contour (Figure 1) [22].

Cystic areas related to distended glands replete with proteinaceous liquid can be observed inside the polyp or this can show up as a nondistinctive endometrial thickening or focal matter into the endometrial lumen (Figure 2) [7].

Also, the argued timing for TVUS is the proliferative stage of the menstrual cycle, and TVUS reassessment after menses can help to distinguish a true polyp from endometrial thickening [8].

In another train of thoughts, the vascularity of EP stems from the uterine vascular system, as a stretched and forked spiral artery. This pattern can be recognized by flow mapping using color or power Doppler mode (Figure 3) [23].

Continuing the investigation, the extended approach of color or power Doppler correspondingly, can enhance the diagnostic performance of TVUS [22]. Color-flow Doppler can evidence the sole nourishing vessel, representative for EP. Power Doppler is noted to rise sensitivity to 91% and 97% in women with and without symptoms (Figure 4) [23].

Three-dimensional TVUS (3D-TVUS) is a noninvasive imaging procedure with the capability to produce multi-planar reconstructed images of the uterus and its outer borders (Figure 5) [7].

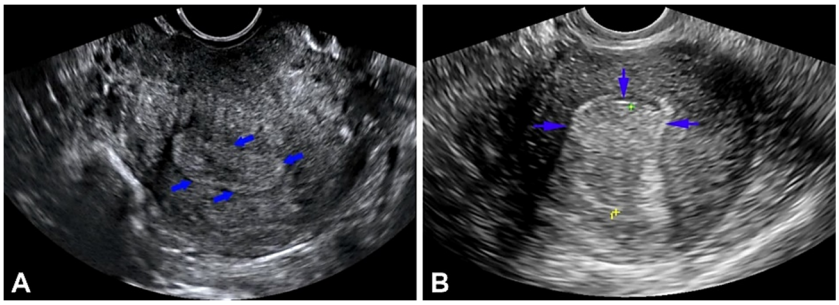


Figure 1 – ***Transvaginal ultrasound demonstrating EP: (A) EP appearing as a hyperechoic image with uniform outlines inside the uterine cavity (blue arrows); (B) EP surrounded by a fine hyperechoic contour (blue arrows). EP: Endometrial polyp.***

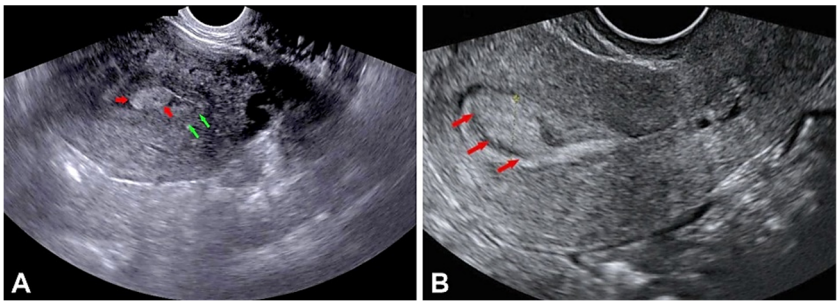


Figure 2 – ***Transvaginal ultrasound demonstrating EP: (A) EP appearing as a hyperechoic image with uniform outlines inside the uterine cavity (green arrows) and cystic spaces within the polyp (red arrows); (B) EP – cystic areas are observed inside the polyp. EP: Endometrial polyp.***

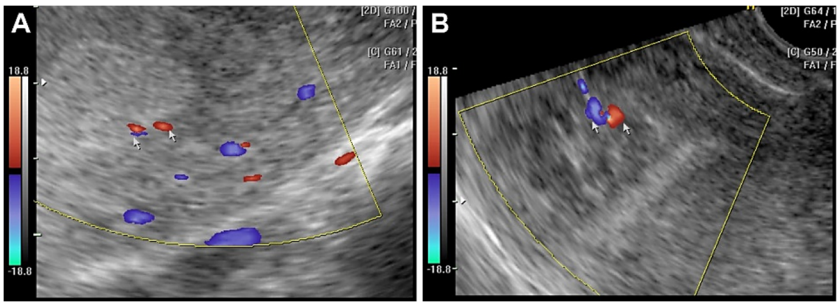


Figure 3 – ***TVUS demonstrating EP: (A) Color Doppler TVUS demonstrating the vascularity of the EP; (B) Color Doppler TVUS demonstrating the vascularity of the EP as an elongated and branching spiral artery. EP: Endometrial polyp; TVUS: Transvaginal ultrasound.***

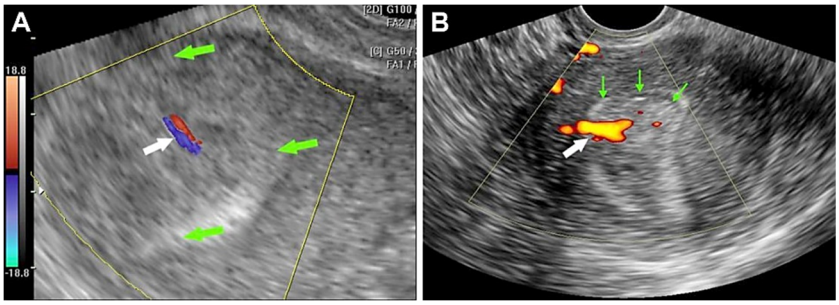


Figure 4 – ***Color and power Doppler TVUS demonstrating EP and the feeding vessel: (A) Color Doppler TVUS demonstrating EP (green arrows) and the feeding vessel (white arrow); (B) Power Doppler TVUS demonstrating EP (green arrows) and the feeding vessel (white arrow). EP: Endometrial polyp; TVUS: Transvaginal ultrasound.***

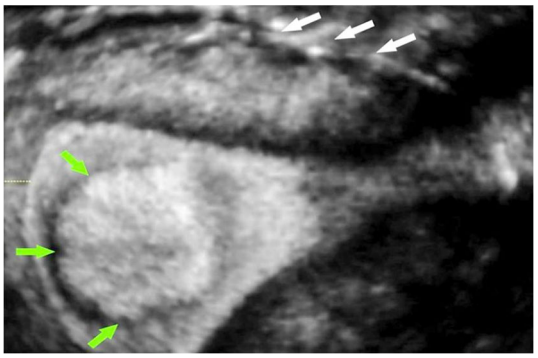


Figure 5 – ***Three-dimensional transvaginal ultrasound demonstrating endometrial polyp (green arrows) and the uterus external contour (white arrow).***

Kupesic & Kurjak consider that one of the most helpful scan planes achieved by 3D-TVUS is the coronal view, which is currently not acquired by TVUS because of the limited mobility of the transvaginal transducer [24]. TVUS and 3D-TVUS with contrast saline infusion sonohysterography (SIS) represent other additional and complementary techniques for the diagnosis of EP.

TVUS–SIS and 3D-TVUS–SIS can delineate reduced EP loosed on grayscale TVUS and is presumptively to refine diagnostic precision [25–29].

Blind biopsy by dilation and curettage is imprecise in EP assessment and must not be accomplished as a diagnostic procedure [7, 30].

The utilization of an endometrial sampler or a curette may lose pedunculated EP and shattering of sessile polyps and may produce difficulties in the histological confirmation [7, 31].

Hysteroscopy and guided biopsy are the best techniques to be compared with other methods for the diagnosis of EP, as it provide the maximal sensitivity and specificity for conservative management [22, 32].

Hysteroscopy with guided biopsy is the "gold standard" in the diagnosis of EP [7, 32]. The basic benefit of hysteroscopy is the capability to visualize and eliminate polyps at the same surgical time (Figure 6) [7].

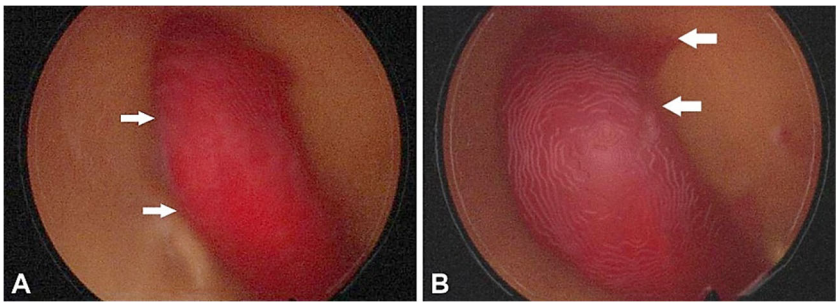


Figure 6 – ***Hysteroscopy in EP: (A) Pedunculated lateral wall EP (arrows); (B) Fundic region sessile EP (arrows). EP: Endometrial polyp.***

EP tissue density is to be considered as the compact tissue will necessitate devices, such as pointed scissors, and simple devices could be improper [33].

Jansen *et al*. [34] note the fact that the complication rates at hysteroscopy are low, referring a general complication rate of 0.28% in 13 600 hysteroscopies; the rate for operative extirpation of EP in this research was 0.4% [7, 34].

Broad-based and sessile EP are usually implanted at the largest size of the polyp, while fundal attachment poses an added difficulty for tissue removal [33].

However, hysteroscopy with guided biopsy is the "gold standard" in the diagnosis of EP, allowing direct visualization, exact localization, and possible simultaneous resection.

Furthermore, other imaging methods, such as magnetic resonance imaging (MRI) and computed tomography (CT)

scan may be useful in the EP assessment, but their utility is diminished either by the high costs or by the sometimes-reduced availability.

As an argument, Salim *et al*. consider that EP can be diagnosed on MRI as reduced signal intensity intracavitary structures encircled by high signal intensity fluid and endometrium by T2-weighted MRI. Also, exceeding charges and limited availability, with limited benefits over TVUS, exclude this method from usual use. CT has a limited performance as of its cost, radiation exposure, and reduced sensitivity [7].

Lastly, the current diagnostic pattern of EP is presented synoptically in Table 3.

Table 3 – ***Current EP diagnostic pattern [4, 22]***

EP diagnostic pattern	TVUS should be used as the diagnostic procedure of choice for the identification of EP in patients of reproductive age [4]. TVUS provides confident details for the detection of EP and should be the examination of choice when accessible [22].
	Diagnostic precision of TVUS is enhanced when color Doppler, 3D reconstruction and contrast are utilized [4].
	Dilation and curettage or other blind intrauterine maneuvers should be avoided for the assessment and management of women with EP [4].
	In office diagnostic hysteroscopy demonstrated the highest diagnostic precision and should be accomplished in infertile women with suspected EP [4].
	EP might alter endometrial receptivity, impairing embryo implantation and reducing pregnancy rates [4].

Adapted from [4] & [22]. 3D: Three-dimensional; EP: Endometrial polyp; TVUS: Transvaginal ultrasound.

EP management

For patients with EP, management is based on symptoms, risk of malignancy, fertility concerns, and physician skills [7].

EP are frequently benign, but they may contain premalignant or malignant tissue remodeling [35].

Starting from the premise that most EP are benign, there is an alternative for expectant management and no surgical treatment [22].

Asymptomatic postmenopausal EP are improbable to be malignant and expectant management is an alternative conditioned by counseling the patient [22, 36].

Medical management has a limited contribution in EP [8, 22]. Medical therapy can have certain contributions in the management of EP and gonadotropin-releasing hormone (GnRH) agonists are referred to offer short-term symptomatic improvement for EP, but symptom iteration is habitual with therapy stoppage [37].

The use of Levonorgestrel-releasing intrauterine system (LNG–IUS) seems to have a role in the medical treatment of EP.

Gardner *et al*. consider that the use of LNG–IUS in patients treated with Tamoxifen is referred to diminish the occurrence of EP [38].

Surgical management can be classified based on conservative and radical surgical methods [22, 39].

Furthermore, Ludwin *et al*. state that conservative management can be onward classified into blind and hysteroscopic methods, while the radical treatment include hysterectomy in patients who have completed family planning [39].

In a somewhat abstract way, it was considered that the conventional therapy for EP is blind dilatation and curettage, this method has been reported to eliminate only 8% of EP, whilst adding polyp forceps rises full removal to 41% [8, 22, 40].

Blind dilation and curettage have been the usual management alternative for AUB and suspected endometrial disorders for many times and is yet usual practice (Figure 7), for the excision of EP, but research advises that this method is inefficient and has a considerable complication rate [7, 41].

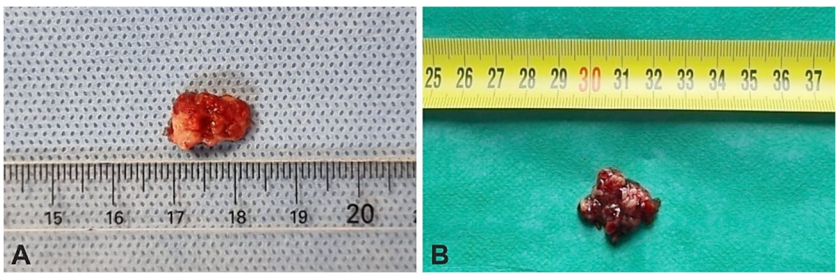


Figure 7 – ***Gross images of blind dilation and curettage of EP: (A) Hyperplastic EP (pathology confirmed); (B) Functional EP (pathology confirmed). EP: Endometrial polyp.***

However, *American Association of Gynecologic Laparoscopists* (AAGL) practice guidelines states the fact that when hysteroscopic approach is accessible, blind curettage should not be practiced as a diagnostic or curative technique in EP. When an EP is diagnosed or suspected and hysteroscopy is not attainable, the patient should be directed for adequate treatment [22].

Hysteroscopic polypectomy is efficacious and reliable as both a diagnostic and treatment method [22]. Also, hysteroscopy allows rapid recuperation, return to common way of life, and short hospital or office stay [42–44].

Polypectomy accomplished with slim-caliber operative hysteroscopes in the office circumstances offers women the advantages of attentive techniques and lower risks than those linked with general anesthesia [33].

However, diagnostic and operative outpatient hysteroscopy is more cost-effective than inpatient hysteroscopy under general anesthesia and enables quick recuperation [8, 45].

The best approach to EP resection is to be aligned to the uterine border, with the operative device having approach to the polyp base at correct angles [33].

The category of instruments used for polyp excision is based on availability, financial plan, and surgical skills, as well as the size and localization of the EP [7, 46, 47].

Presently, there are a diversity of techniques available for hysteroscopic treatment in EP, comprising electrosurgical removal, grasper-scissor resection, mechanical morcellation or the use of diode laser [8, 22, 33].

Nonetheless, no single hysteroscopic set-up and technique should be considered as preferred over others considering the efficacy, reliability, and costs to speculate its use in all patients [8, 33, 39, 46, 48, 49].

Intrauterine adhesion risk is reduced after hysteroscopic polypectomy, as the myometrium is not incised, and more than that, Taskin *et al*. [50] consider that there are no adhesions after hysteroscopic polypectomy [51].

However, polypectomy complications are classified into those linked to hysteroscopy in general and those connected to a distinctive technique or instrument [8, 52].

Hysterectomy is the definitive treatment for EP (Figure 8) [7, 22]. As well, hysterectomy assures no EP reappearance and no possibility of malignancy [22].

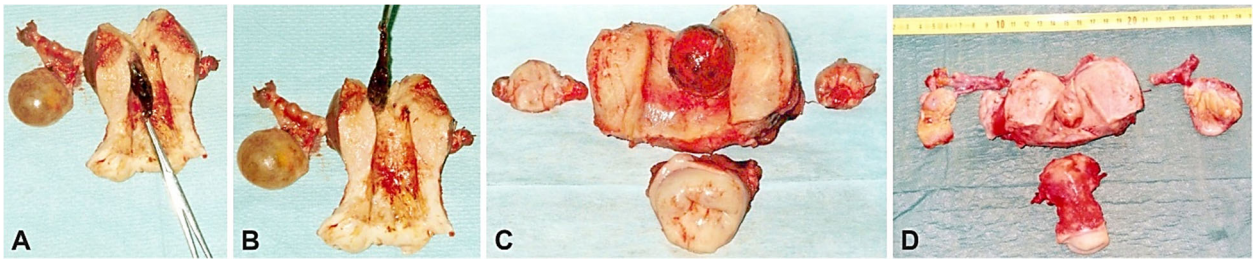


Figure 8 – ***Hysterectomy specimens: (A and B) Hysterectomy specimens demonstrating large sessile EP; (C) Hysterectomy specimen demonstrating bottom and left side voluminous and bulky pedunculated EP; (D) Hysterectomy specimen demonstrating bottom and right side voluminous and bulky pedunculated EP. EP: Endometrial polyp.***

Obviously, it is an extensive surgical technique, with remarkably potential for morbidity and higher costs and it should be used properly and only after counseling women regarding its implication [7, 22, 53].

Morphology and surgical pathology of EP

From a histogenetic point of view, the development of EP is based on the exaggerated monoclonal growth of endometrial stromal cells and the secondary induction of the benign polyclonal growth of the glands [3].

The definite causes of EP are currently unspecified, even though risk factors for their development according to studies include increasing age, Tamoxifen, hypertension, and obesity [54–57].

The chromosomal analysis of the stroma of polyps reveals in most cases clonal translocations involving areas 6p21-p22, 7q22 and 12q13-15 from regions 2–5 [3, 58].

EP are recognized when they manifest as gross, cauliflower-like structures (Figure 9) within the endometrial cavity, they are much more frequently seen as microscopic, often clinically unsuspected findings in curettage specimens (Table 4) [59].

Table 4 – ***EP morphology***

EP morphology	A solid unfragmented structure.
	A smooth contour, covered on three aspects by surface epithelium.
	A focally or diffusely fibrotic stroma.
	Scattered cystically dilated glands.
	Thick-walled sclerotic blood vessels.

Adapted from [59]. EP: Endometrial polyp.

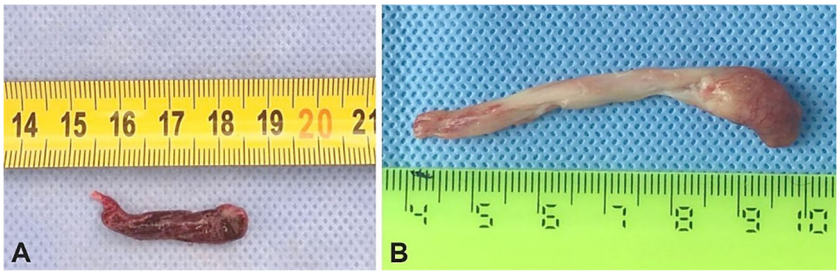


Figure 9 – ***Gross appearance of EP: (A) Pedunculated EP demonstrating gross, cauliflower-like structure; (B) Pedunculated and significantly elongated EP demonstrating smooth and bosselated surface. EP: Endometrial polyp.***

Often, the first indication to the presence of a polyp in a curettage specimen (Figure 7) in the remark that a fragment of tissue is present that appears certainly different to the other endometrial fragments on the slide and the basis for this discordance is that the EP usually respond only partially or not at all to the normal hormonal background and thus contain endometrium that may be atrophic or poorly proliferative, despite a fully proliferative or secretory model in the surrounding nonpolypoid endometrium [59–62].

Ciscato *et al*. found a certain histological pattern that is found in different ways in EP (Table 5) (Figures 10–15) [54].

Silverberg & Tabbara state that the most important differential diagnosis of the EP by curettage specimen is with well-differentiated endometrial carcinoma invading the myometrium [59].

Also, another important differential diagnosis is with the atypical polypoid adenomyoma [59, 63–68].

Furthermore, cellular polyps with mitotically active stroma may also be confounded with adenosarcoma, but absence of the periglandular hypercellular stromal cuffing distinctive of that lesion [59, 68].

Table 5 – *EP histological pattern*

EP histology	Stromal atypia, explained as pleomorphism, and categorized as mild, moderate, and severe.
	Glandular crowding, explained as the existence of discrete foci measuring at least 0.5 mm whither gland/stroma proportion overrunned 50%, and which was devoid of any cytological delimitation.
	Infarction, explained as zones of necrosis, sharply defined zones of acellular hyalinization, and diverse other changes [63].
	Periglandular condensation of stromal cells, distinct from the background away from glands.
	Diffuse stromal hypercellularity, explained as a level of cellularity that is similar with endometrial stroma in the proliferative stage in most of the polyps.
	Prominent thick-walled vessels in most fragments of the polyp.
	Bizarre stromal cells, different from severe atypia, based on multinucleation concurrent with hyperchromasia [64].
	Stroma predominant fragments, explained as EP fragments with only minimal (<10%) epithelium.
	Intraglandular stromal papillation, explained as stromal protrusion within glandular spaces irrespective of the extent [65].

Adapted from [54]. EP: Endometrial polyp.

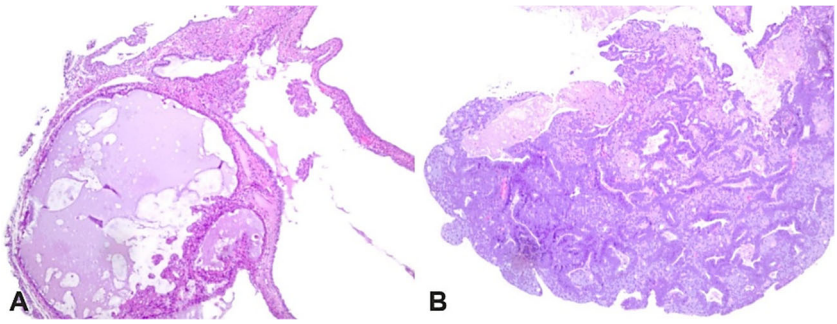


Figure 10 – ***(A) Atrophic polyp – dilated glands with low columnar to cubical epithelial lining, fibrotic stroma; (B) EP – closely packed tubular, irregular and branching glands lined by columnar epithelium, with conspicuous elongated nucleoli, without atypia, showing foci of squamous metaplasia. HE staining: (A and B) 40×. EP: Endometrial polyp; HE: Hematoxylin–Eosin.***

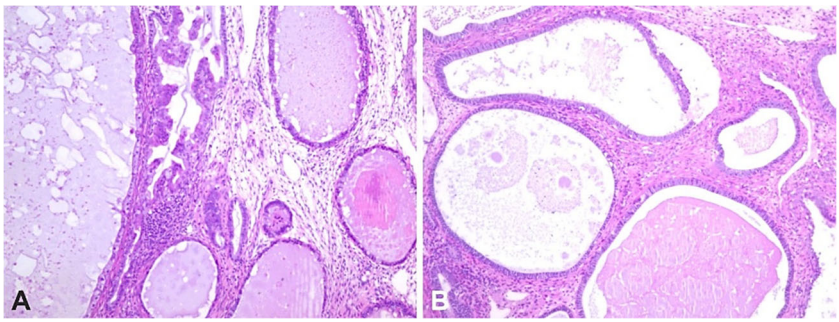
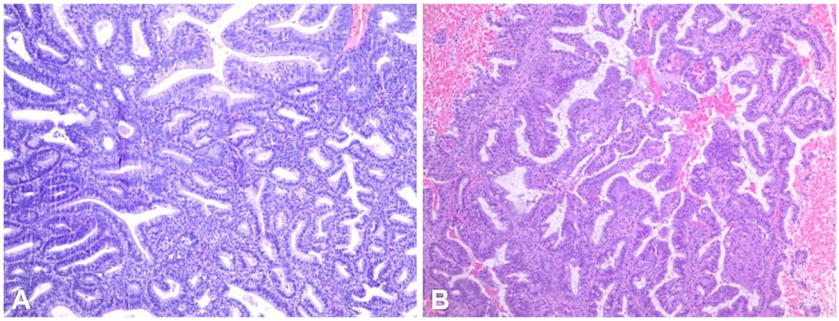


Figure 11 – ***(A) EP – dilated glands with low cubical epithelium and area with mucinous metaplasia, stroma with edema and inflammatory infiltrate; (B) EP – dilated glands with epithelium with tubal-type ciliated cells associated with endometrial hyperplasia. HE staining: (A and B) 100×. EP: Endometrial polyp; HE: Hematoxylin–Eosin.***

Figure 12 – ***(A) Hyperplastic EP – polypoid endometrial mucosa with closely packed tubular and irregular glands lined by pseudostratified columnar epithelium, without cytological atypia, reduced with fibrotic stroma with hyperemic vessels; (B) EP – crowded endometrial glands with secretory differentiation, pseudopapillary projections inside the lumina, fibrotic stroma. Hematoxylin–Eosin (HE) staining: (A and B) 100×. EP: Endometrial polyp.***



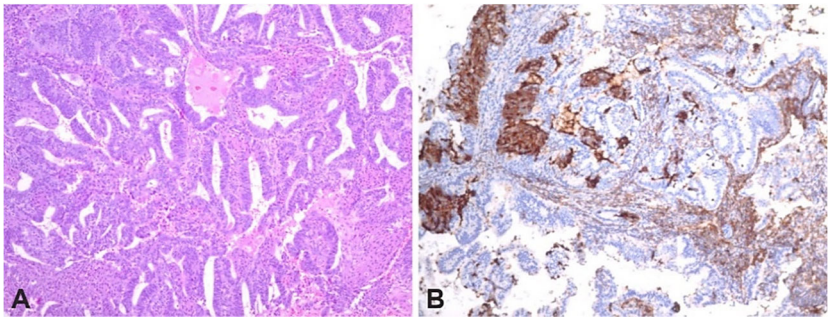


Figure 13 – ***(A) Hyperplastic EP – irregular glands lined by columnar epithelium, with conspicuous elongated nucleoli, without atypia, showing foci of squamous metaplasia; (B) Hyperplastic EP – CD10 positive in the endometrial stroma and in the squamous epithelium. Hematoxylin–Eosin (HE) staining: (A) 100×. Immunohistochemical labeling with anti-CD10 antibody: (B) 40×. CD10: Cluster of differentiation 10; EP: Endometrial polyp.***

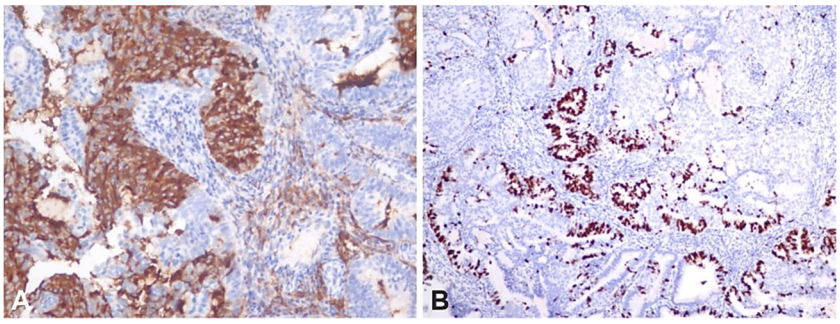


Figure 14 – *(A) Hyperplastic EP with squamous metaplasia – CD10 positive in the squamous morules; positive reaction to IHC staining; (B) EP – Ki67 positive in the epithelial cells, hot spot positivity approximately 80%; positive reaction to IHC staining. IHC labeling with anti-CD10 antibody: (A) 100×. IHC labeling with anti-Ki67 antibody: (B) 40×. CD10: Cluster of differentiation 10; EP: Endometrial polyp; IHC: Immunohistochemical.*

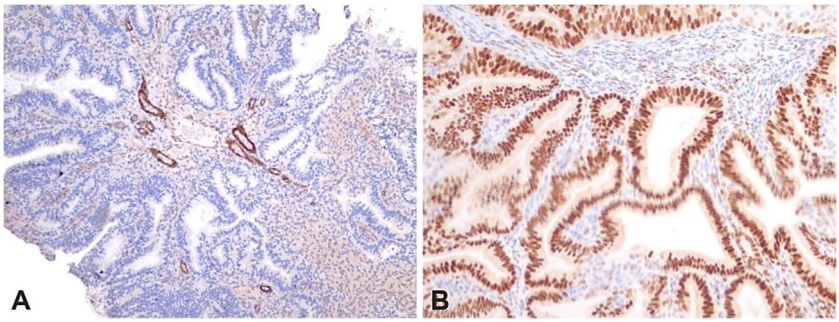


Figure 15 – *(A) EP – actin positive in the vessels; positive reaction to IHC staining; (B) EP – ER positive in the epithelial cells; positive reaction to IHC staining. IHC labeling with anti-SMA antibody: (A) 100×. IHC labeling with anti-ER antibody: (B) 200×. EP: Endometrial polyp; ER: Estrogen receptor; IHC: Immunohistochemical; SMA: Smooth muscle actin.*

EP and the risk of malignancy

Even if the most EP are benign, they can get hyperplastic, with malignant degeneration, developing in 0–12.9% of polyps in case series reported so far [7, 9, 25, 36, 69–72].

On the other hand, Jacobs *et al*. find that the incidence of endometrial carcinoma in hysterectomy specimens after the diagnosis of endometrial atypical hyperplasia in random endometrial biopsy is about 40% [73–75].

However, the risk of EP malignancy is higher in the presence of AUB among symptomatic than asymptomatic women, age over 60 years, menopausal status, hypertension, diabetes mellitus, Tamoxifen use and obesity are significantly associated with malignancy (Figures 16 and 17) [4, 76–79].

Moreover, Lieng *et al*. found that the most remarkable issue is that the risk of malignancy found in EP is highest in postmenopausal patients with symptoms [35].

The risk of hyperplasia and malignancy in EP is higher in postmenopausal women presenting a thickened endometrium and consequently, these patients should be further investigated ideally with hysteroscopic-guided biopsy [4, 80].

In this regard, Vitale *et al*. have developed a guide and recommendations for women presenting EP suspected of malignancy (Table 6) [4].

Overall, the risk of malignancy is reduced in premenopausal patients, but it has been remarkably linked with increasing age and menopause [7, 81].

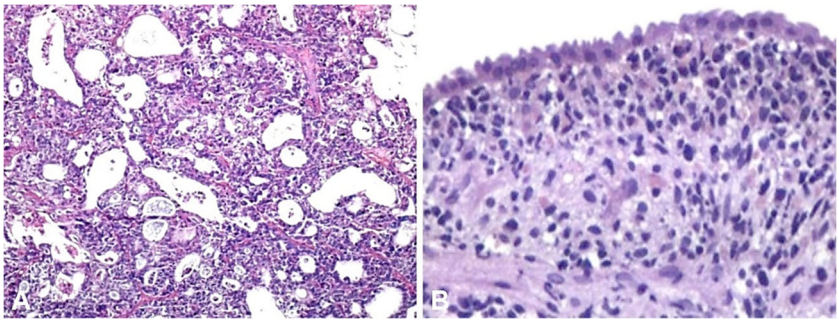


Figure 16 – *(A) Clear cell carcinoma in a polyp – polypoid structure with proliferation of polygonal cells, with moderate to abundant cytoplasm, hobnail cells and moderate cytological atypia; (B) Adenosarcoma – biphasic tumor with admixed glands and prominent stroma, periglandular stromal condensation, leaf-like architecture. HE staining: (A) 40×; (B) 100×. EP: Endometrial polyp; HE: Hematoxylin–Eosin.*

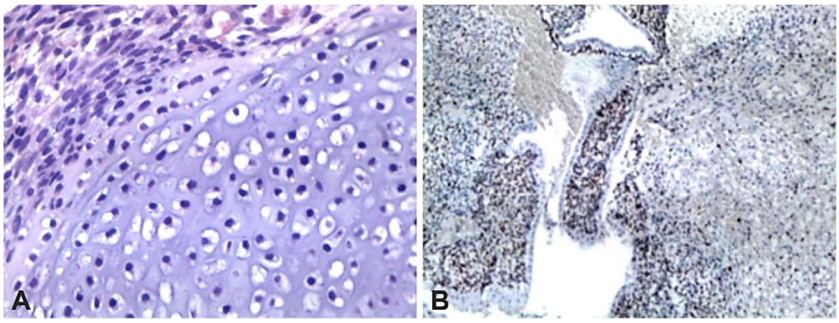


Figure 17 – *(A) Adenosarcoma – stroma with heterologous differentiation (cartilage); (B) Adenosarcoma – Ki67 positive in stroma; positive reaction to IHC staining. HE staining: (A) 100×. IHC labeling with anti-Ki67 antibody: (B) 100×. EP: Endometrial polyp; HE: Hematoxylin–Eosin; IHC: Immunohistochemical.*

Table 6 – ***Guidelines and recommendations for women presenting EP suspected of malignancy***

Guidelines and recommendations for EP suspected of malignancy	Postmenopausal women with vaginal bleeding and a suspected EP should undergo diagnostic hysteroscopy with hysteroscopic polypectomy if an EP is visualized.
	Contrast SIS is highly precise in identifying EPs in asymptomatic postmenopausal women.
	Office hysteroscopy has the highest diagnostic precision with high cost-benefits ratio for premalignant and malignant pathologies of the uterine cavity.
	Dilatation and curettage should be avoided due to their imprecision in identifying polyps and malignancies.

Adapted from [4]. EP: Endometrial polyp; SIS: Saline infusion sonohysterography.

EP and the risk of recurrence

The described recurrence rates of EP after hysteroscopic resection range from 0–43.6% in the literature, depending on the type of polyp resection technique, the number of EP, and the follow-up period [43, 54, 82, 83].

The possible clinical risk factors that can bias the incidence of recurrences are parity, body mass index, age, hypertension, diabetes mellitus, hormone replacement therapy or Tamoxifen therapy [83].

Furthermore, the risk of recurrence seems to be independent of the existence of AUB, and the menopausal status also is being suggested to be independent by the number and diameter of the polyps [11, 83].

EP and clinical outcome

Clinical outcomes after treatment of EP are generally favorable and the symptomatic improvement is excellent, with AUB remitted after hysteroscopic polypectomy [7, 84].

Polyp resection improves AUB remission, life quality, fertility, and malignancy detection [8].

However, Nathani & Clark specified a symptomatic amelioration in 75–100% of the patients in a two to 52-month follow-up [85]. The resection of EP by surgical techniques results in the life quality improvement, with a reduction in patients' AUB symptoms [8, 86–89].

Conclusions

EP are a frequent gynecological condition. Increasing age, hypertension, hyperestrogenism, and Tamoxifen use are acknowledged as habitual risk factors for the appearance of EP. Symptomatic polyps typically cause AUB. TVUS is the primary investigation in EP, especially in the presence of AUB or infertility. Color-flow or power Doppler can improve the diagnostic efficiency of TVUS. One of the most useful scan planes obtained with the 3D-TVUS is the coronal view. Surgical management can be classified based on conservative and radical surgical methods. Hysteroscopic resection is now the "gold standard" to treat the EP. Hysteroscopic polypectomy is efficacious and reliable as both a diagnostic and treatment method. Outpatient hysteroscopy is more cost-effective than inpatient hysteroscopy under general anesthesia. Hysterectomy is the definitive treatment for EP, but it requires a judicious indication and an adequate counseling of the patient. Currently, a certain histological pattern is found in different sequences in EP. Even if the most EP are benign, they may become hyperplastic, with malignant transformation. The risk of hyperplasia and malignancy in EP is higher in post-menopausal women presenting a thickened endometrium. Risk factors that may influence the incidence of recurrences are parity, body mass index, age, hypertension, diabetes mellitus, hormone replacement therapy or Tamoxifen treatment. Clinical outcome after treatment of EP is generally favorable.

Conflict of interests

The authors declare that there is no conflict of interests regarding the publication of this paper. All authors read and approved the final manuscript.

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