

Management of endometrial polyps

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Abstract

The epidemiology of endometrial polyps is reported to be between 7.8 and 50% of women. The range remains quite broad and inconsistent due to confounding study factors such as the method of research, population studied, histological type and anatomical location of polyps. The development of polyps is influenced by a multitude of genetic and epigenetic factors. Chromosomes 6,7 and 12 are incriminated in this process. A fraction of these polyps may undergo malignant transformation, most commonly in postmenopausal patients. 3D ultrasound (US) and hysterosalpingo-contrast-sonography (HyCoSy) provide an accurate diagnosis and location of endometrial polyps (EPs). Expectant management is recommended when the polyp is up to 10mm in length, in asymptomatic young patients. When indicated, hysteroscopic removal of polyps can be performed as an outpatient without requiring a general anaesthetic. The use of a small tip diameter hysteroscope and 5Fr instruments offers safe, efficient and low-cost treatment. The hysteroscopic morcellator and shaver are the best surgical option for bigger polyps since it is a quick and time-effective method with the technique easily learned by surgeons.

Key words: endometrium; polyps; meysteroscopic; alignancy; polypectomy; infertility.

Introduction

Endometrial polyps (EPs) present hyperplastic growths of stroma and endometrial glands [1]. The loss of apoptotic regulation and the overexpression of estrogen and progesterone receptors are seen in both premenopausal and postmenopausal women [2]. These are generally asymptomatic, incidental findings discovered during ultrasound scanning; symptoms include bleeding or abnormal vaginal discharge. Approximately 25% of postmenopausal women with EPs will have abnormal uterine bleeding (AUB). Women on cyclical HRT might have irregular or heavy „menstrual' bleeding. In premenopausal patients“ EPs can cause infertility [3]. Polyp occurrence appears to depend on many genetic alterations, in conjunction with metabolic, drug induced, and environmental factors. The involvement of various factors has been reported including: enzymes, diabetes mellitus, obesity, hypertension, age, menopause status and steroid hormone receptors [2,4]. Rearrangements in the 6p21-22, in the 12q13-15, and in the 7q22 region [5] and the involvement of bcl-2 and bax apoptosis related genes have been shown to play a role in the evolution EPs. Analysis of EPs showed an increased bcl-2/bax ratio that could ultimately be responsible for a mechanism that promotes their growth [6].

The histological structure of EPs contains an amalgamation of large thickened blood vessels, variably formed glandular spaces and fibrous stroma. They can develop into cancer (infrequently), become atrophied or remain benign [1]. Classification by tissue type is another way to categorise polyps: adenomatous (most common), cystic, fibrous, vascular, inflammatory, and fibromyomatous. Di Spiezio Sardo et al. [7] contrastingly labelled the possible types as: hyperplastic, atrophic, functional, adenomyomatous and pseudopolyps.

Effects of Polyps in the Endometrial Cavity

Hysteroscopic features such as endometrial erosion, vascular dilatation [6] and chronic endometrial inflammation have been identified in women with EPs [2].

The locations of resected polyps are usually the anterior and posterior walls with the fundus being the third most common location [8]. The locality of a polyp is of considerable importance when addressing fertility issues. For instance, the removal of tubocornual polyps ameliorates the pregnancy rate to a higher degree when compared to those removed polyps from the lower 1/3 of the uterine corpus [2,9].

The higher miscarriage rate in women with EPs may be attributed to an increased production of glycodeilin that can inhibit the action of natural killer cells and additionally reduce blood flow to endometrial lining. Other factors may result in abnormal uterine bleeding such as vascular fragility, surface erosion, ischemic necrosis, and disruption of sub-surface capillaries [10,11].

Epidemiology

EPs are the most frequently diagnosed type of polyp of the female genital tract. The older the patient, the higher the incidence, to some extent. Numbers reach their peak incidence during the 6th decade and decline thereafter, following menopause. Their prevalence ranges from 7.8-34.9% in varying populations [7,12]. EPs incidence in patients with abnormal uterine bleeding is 7.8%, [13] however it is estimated to be 10% in women with no abnormal bleeding [14]. Risk factors for the development of EPs include age, diabetes, hypertension, obesity, and tamoxifen use [15,16]. The prevalence of post-menopausal polyps reaches to up to 6% depending on the population studied. There is an increased incidence (8-36%) in women on tamoxifen and HRT [16-18]. Interestingly, a new study assessed the prevalence of colorectal polyp in postmenopausal patients with EPs [9] finding a high incidence of colorectal polyps in patients who also had concomitant EPs [19]. Alike the resection of EPs for relief of symptoms or restoration of fertility, colorectal polyps may be detected and also removed in order to avoid troublesome manifestations or malignant transformation [1,13]. In premenopausal women, polyps most frequently cause abnormal uterine bleeding (AUB) but abdominal pain is also a common finding. However, polyps may be incidentally identified in completely asymptomatic patients [8].

Diagnosis of Polyps in Pre-menopausal Women

The routine use of trans-vaginal ultrasound (TVU) has increased diagnostic accuracy and the number of patients found to have polyps [20]. EPs are most often detected on the 10th day of the menstrual cycle. False-positive and false-negative results are reduced when EPs are screened on a thin layer of endometrium [9]. The use of a contrast saline infusion sonography (SIS), gel installation sonography (HyCoSy), and hysteroscopy are the means to confirm diagnosis. Hysteroscopy remains the gold standard for diagnosis and treatment of EPs [9]. Occasionally, the curettage can provide endometrial sampling from the remaining endometrium after excision of the polyp [21].

Expectant Management

Small and asymptomatic EPs incidentally found by TVU in young women are managed conservatively due to the low incidence of malignancy [8], particularly it is less than 10mm. Data has also shown that up to 25% of polyps below 10 mm may regress spontaneously [22]. Salim et al. [9] found that the likelihood of EPs regression is linked to their size when monitored for 1 year. EPs of 15.1mm of length were less likely to regress compared with those measuring approximately 10.7 mm. Consequently, polyps may be removed in symptomatic patients, but polyps in patients whom have no presenting symptoms and are of smaller size - conservative management with regular follow-up should be a well-considered alternative.

The Management of Endometrial Polyps in Infertility

EPs are frequently seen among sub-fertile women. Their presence has been found to be directly related to decreased fertility [23]. The exact incidence of EPs in infertile population is not known. It is estimated to be around 6-15 % in sub fertile women with regular menses and c32 % in the total infertile population [24]. The incidence of polyps diagnosed by hysteroscopy is 16.5-26.5% in women with unexplained infertility, up to 46.7% in infertile women with endometriosis, and 0.6 % to 5% in women with recurrent pregnancy loss [17,25].

Successful implantation requires a receptive endometrium synchronized to the embryonic age. EPs compromise endometrial receptivity and implantation by select mechanisms. Implantation is compromised by the presence of a polyp due to the asynchronisation of the hormonal response normally elicited by a functioning endometrium. Moreover, the levels of endometrial markers involved in the processes of decidualisation, implantation and trophoblast invasion are affected when EPs are present. [26] The concentration of glycodelin is also of great significance since it has an inhibitory effect on spermocyte binding. In healthy patients it stays low throughout the peri-ovulatory period and rises only during implantation. However, in EP patients, glycodelin secretion is augmented during the follicular phase [27]. Other markers linked to endometrial receptivity include tumor necrosis factor alpha (TNF α) and insulin-like growth factor binding protein-1 (IGFBP-1) these factors have shown to be at decreased levels in the mid-secretory phase when EPs are present. These concentrations are subsequently normalised after polypectomy [25]. Tubal ostia polyps mechanically impair the sperm and/or embryo from migrating to the uterus. Resection of the utero-tubal junction EPs has the highest impact on pregnancy outcome in ovulation induction and intrauterine insemination (IUI) cycles [27].

Conception After Polypectomy

In symptomatic women with no other recognized reason for infertility, hysteroscopic polypectomy increases pregnancy rates independent of the polyp size [28]. Furthermore, excision of polyps with a mean size of 26 mm prior to referral to first Intrauterine Insemination (IUI) was found to increase spontaneous pregnancy rate. The likelihood for a clinical pregnancy is increased in women set to undergo a polypectomy, if they have been referred for IUI as a consequence of unexplained female or male factor infertility. [29]. In asymptomatic women, due to the lack of further supporting evidence, conservative management has been suggested to be considered small EPs. Nevertheless, it is advisable to excise polyps if they are discovered before beginning Intra-Cytoplasmic Sperm injection (ICSI) or In Vitro Fertilization (IVF) treatment [30].

Paradoxically, several studies have reported that newly diagnosed EPs less than 1.5-2 cm in diameter during controlled ovarian hyper-stimulation (COH) do not have an adverse impact on live birth rates after fresh embryo transfer [31]. On the other hand, in cases of recurrent IVF failure, an increase in cumulative pregnancy rate was noted once hysteroscopy was performed prior to subsequent IVF/ICSI [32]. An interval of >1 menstrual cycle between surgical excision and subsequent IVF cycle is advised when polypectomy is indicated. [33].

Diagnosis and management of polyps in postmenopausal women

Despite the malignant potential of EPs being low, rates can reach 12.9 % depending on the population studied. [34] Concerns around malignancy are often raised in postmenopausal women. When patients are not under hormonal treatment, a polyp developed in an atrophic postmenopausal endometrium could be suspicious. However, women may have had undiagnosed benign polyps before they become menopausal. Further research is needed to identify whether there is a subgroup of these women that are at higher risk of malignancy. Diagnostic tools are identical for both pre- and post-menopausal women. EPs closer to the tubal origin are more linked with malignancy [7]. Hysteroscopy remains the gold standard for diagnosis and treatment allowing also the final histological diagnosis [35].

Risk of Malignancy

Post-menopausal bleeding is linked to the most augmented risk of pre-cancerous and malignant tissue changes [7] [21]. The majority of authors are in consensus that the likelihood of malignancy in EPs heightens with age [15,27]. Moreover, vaginal bleeding increases the potential for malignant change of EPs when paralleled with asymptomatic non-bleeding women [18,35,37]. There is a higher rate of simultaneous endometrial hyperplasia with EPs [38], particularly in women taking HRT [18], this should also be taken into consideration in the management plan.

Post-menopausal polyps that are asymptomatic are not likely to be malignant and further observation is a potential management plan following discussion with the patient. With regard to small EPs <5mm, there is no unanimity on when is best to offer surgical treatment [18,37]. Further studies are necessitated to gain an understanding as to whether incidental EPs of 10mm in asymptomatic postmenopausal women can be treated without surgery in a safe manner [39]. In addition, removing a polyp from atrophic endometrium will most likely not provide any secondary prevention from endometrial cancer [18,37]. Follow-up and/or treatment of EPs that are incidentally diagnosed in postmenopausal patients, who are asymptomatic, could be safely limited to select number of cases based on polyp characteristics such as shape and diameter. Regarding prevention in tamoxifen or oestrogen treated patients, intrauterine systems (Levonorgestrel releasing) could potentially have a preventative function in polyp formation [40]. Though rare, atypical hyperplasia as well as endometrial cancer may begin as EPs. The results of case series indicate that malignancy occurs within 0%-12.9% of EPs [18,36,37].

Pre-operative Workup

The diagnostic accuracies of sonohystero-graphy and hysterosalpingogram (HSG) are 52% and 60% respectively. Despite HSG having a high sensitivity for intrauterine lesions, the technique is unable to differentiate submucosal myomas from EPs [39]. 3D Ultrasound (US) and contrast sonography both have exceptional sensitivity. They better identify the precise locality and size of EPs when compared to 2D TVU [41]. The gold standard however for polyp diagnosis is hysteroscopy since it provides simultaneous management under direct observation [42].

Hysteroscopic Polypectomy Techniques

Different hysteroscopic methods are used for polyp removal including mechanical and electrosurgical techniques; however, there are no studies comparing these methods, assessing costs or efficacy. The method of choice remains the one most familiar for the surgeon, the one they have most experience and training with. Cells of a malignant nature at the polyp base may be missed with blind avulsion techniques e.g. endometrial curettage.



Hysteroscopic resection of EPs under direct vision is a safe and simple technique and can be performed nowadays in an outpatient setting. Recurrence rates are reported to be 15% after blind removal techniques, but hysteroscopic resection guarantees a zero-recurrence rate [35]. Hysteroscopic resection circumvents unnecessary cervical dilatation, diminishes the risk of uterine perforation as well as the risk of false passage creation, chiefly in atrophic post-menopausal uteri [43]. Newer treatment modalities such as hysteroscopic morcellation are now available [44]. Similarly to laparoscopy, hysteroscopic morcellation raises a question mark towards the risk of dissemination of malignant cells [45].

Polypectomy in an Outpatient setting

Mechanical surgery with 5Fr (1French = 0.33mm) bipolar twizzle/ball/needle for small polyps is advocated. Hysteroscopic polypectomy in an office setting is achievable, safe and efficient, additionally it has high patient co-operation and a low recurrence rate. It may be performed without anaesthesia, with para-cervical block, or with conscious sedation. Different techniques according to localization, anatomical aspects, and size of the polyps, can be used.

EPs of 0.5 cm in length may be removed whole [2] with 5Fr forceps or a 5Fr tenaculum post-resection at the base with 5Fr. micro scissors. EPs larger than 0.5 cm may be cut from the free edge to the base in portions, by bipolar and/or twizzle electrode. Fundal polyps may be removed by slicing the base in its entirety, while avoiding going into the myometrium [46]. Electrosurgery or a merged technique is also possible in an ambulatory situation. Contrastingly, the methods available for resection and evacuation of large EPs include: shavers, hysteroscopic morcellators and resectoscopes. For larger polyps or when surgeons have little operational exposure, it is preferable to perform polypectomy under general anaesthesia. Otherwise, a bipolar resectoscope may be utilised, usually also under general anaesthesia via a laryngeal mask. Irrespective of the technique used in an operating room or in ambulatory set up, hysteroscopic polypectomies are regarded as day case surgeries. EPs resected by hysteroscopic loops are viewed as the gold standard technique for sizeable polyps >2 cm. Glycine or mannitol/sorbitol are used as expanding fluids. The key shortcomings with monopolar resectoscopes are fluid overload syndrome and ultimately pulmonary oedema, coagulopathy, cerebral oedema, hyponatraemia, hypochloroemia, and acidosis. The use of a monopolar resectoscope creates a higher risk of uterine perforation versus bipolar systems [47]. Utilisation of bipolar resectoscopes allows the distending fluid to be Ringer's lactate solution or normal saline. The bipolar resectoscope has lower risk of complications although the risk of water intoxication is possible when fluid deficit is over 1.5 L [47].

Regardless of their differences both mono- and bi-polar resectoscopic polypectomy techniques involve chip removal, problematic visualisation, mandate high skills and impose a very steep learning curve. Recent technological advancements with the development of hysteroscopic morcellators and shavers offers new surgery modalities for polypectomy that are equally efficient, similar to resectoscopes, faster, require less skill and a gentler learning curve [48-50]. The resected pieces are destroyed and automatically removed from the uterus, resulting in a clear cavity. Simultaneously, high-speed rotational movements of the instrument tip act mechanically causing haemostasis in the area, subsequently closing micro vessels. Additionally, due to its mechanism of action the endometrial lining is left intact. This is an extremely important facet in the case of large polyps in the fundal area. The base should be completely removed without injuring the sub-endometrial area. The MyoSure system is a one-use tool with a rotational and vertical slicing tip. The Intrauterine Bigatti Shaver (IBS) has multi-use rotating tips [51].

Techniques used to perform a mechanical polypectomy include the use of hysteroscopic scissors, an intrauterine morcellator and bipolar electro-surgical tools [9]. When intrauterine morcellation is compared to bipolar resection of polyps, the former seems to be linked to a lower recurrence of EPs [53].

Scarring of the endometrium may reduce fertility potential and a thin endometrium has been associated with low pregnancy rates in assisted reproductive techniques [54]. Kogan et al. [55] assessed the effect of intrauterine thermal injury caused by bipolar energy on endometrial thickness through a retrospective study; they looked women with a diagnosed intrauterine pathology at the time of enrolment onto an IVF program. Thermal injury through polypectomy had no effect on subsequent endometrial development; endometrial thickness following surgery was decreased from 10.7 mm to 9.5 mm but pregnancy rates still improved from 19.5% to 24.4% [53].

As current evidence fails to demonstrate superiority of any method used for hysteroscopic polypectomy and more importantly, since no comprehensive trials on infertile women are available, the surgical technique for hysteroscopic polypectomy should be chosen according to the surgeon's preference and expertise.

Discussion

Due to differences in selection criteria in available literature, the frequency of EPs in infertility cases as compared to gynecological cases is inconsistent. Nevertheless, the presence of multiple EPs is more common in fertility cases, 35.4% as compared to gynecological cases, 12-20%. Diagnosis of EPs and their exact localization and size are well defined with recent technological advances made in imaging, such as 3D US. In infertility cases, the average size in length of EPs has been reported to be 19 ± 14 mm. It may be inferred that the identification of smaller endometrial polyps is subsequently increasing the number of patients that will ultimately require treatment. The most frequent polyp location is the posterior wall for both EPs in gynecological 39% and infertility cases 32%. The risk of cancer when an EP is present appears to be 10-fold higher in menopausal women versus women of fertile age. There are no set standards detailing the timing of polyp excision in young, asymptomatic women. In symptomatic polyps, physicians utilise different treatment modalities. Hysteroscopic resection has been coined as the "gold standard" treatment, yet it is not the method of choice for some physicians due to lack of resources and training. Recurrence rates are higher in blind removal techniques. More PRCTs on polyps are needed to further standardize the management of EPs .

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