The management of endometrial polyps in the 21st century

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Key content
- Hysteroscopic endometrial polyp removal appears to be superior to the current practice of blind avulsion.
- Outpatient treatment is safe, cost effective and well tolerated, even in older or nulliparous women.
- New technologies facilitate office hysteroscopy.
- Benign endometrial polyps can regress and rarely progress to malignancy.

Learning objectives
- To learn how to diagnose and treat endometrial polyps in pre and postmenopausal women.
- To be able to compare the performance of diagnostic modalities.
- To understand the role of outpatient vaginoscopy and hysteroscopy.

Ethical issues
- Given the cost effectiveness and acceptability of office ambulatory diagnostic and interventional hysteroscopy, is it ethical not to offer such a service?

Keywords cost effectiveness / infertility / malignancy / outpatient hysteroscopy / ultrasonography

Introduction

Endometrial polyps are localised hyperplasic overgrowths of endometrial glands and stroma which form projections from the surface of the endometrium. They can be single or multiple and range from a few millimetres to several centimetres.

With the increased use of pelvic ultrasonography as a basic investigation for gynaecological conditions, incidental endometrial polyps are diagnosed more frequently, which can pose a dilemma for women and for gynaecologists. The presence of endometrial polyps in postmenopausal women can lead to anxiety about malignancy, even though the malignant potential of endometrial polyps is low. The question is whether incidental and asymptomatic endometrial polyps should always be removed and how, and whether there is a subgroup of women at higher risk of malignancy.

Aetiology and presentation

The aetiology of endometrial polyps is unknown, but their close relationship with the background endometrium is demonstrated by the similar way in which they proliferate and express apoptosis-regulating proteins during the menstrual cycle. However, in both pre and postmenopausal women, endometrial polyps lose their apoptotic regulation and overexpress estrogen and progesterone receptors, thus avoiding the usual control mechanisms.

Endometrial polyps are generally asymptomatic and may be an incidental finding during pelvic ultrasonography. However, they present in approximately one-quarter of symptomatic pre and postmenopausal women. Half of the premenopausal women may present with menorrhagia; other presentations include postmenopausal bleeding, prolapase through the cervical ostium, abnormal vaginal discharge and breakthrough bleeding during hormonal therapy.

Epidemiology and risk factors

Endometrial polyps are rare among women under the age of 20 years. The incidence rises steadily with increasing age, peaks in the fifth decade of life and gradually declines after the menopause. Depending on the population studied, 24–41% women with abnormal uterine bleeding and 10% of asymptomatic women are diagnosed with endometrial polyps. Ten percent of women are found to have endometrial polyps at autopsy.

A number of studies report an increased incidence of endometrial polyps in women on hormone replacement therapy (HRT) and tamoxifen (8–36%), which acts as a selective receptor modulator and estrogen agonist on the endometrium. The influence on endometrial polyps seems to be through estrogen, on which endometrial polyps depend. However, endometrial polyp formation appears to be related to the type and dosage of the estrogen and progestogen in HRT; in particular, a progestogen with high anti-estrogenic activity.
may have an important role in preventing the development of endometrial polyps.\textsuperscript{9}

Nappi \textit{et al.}\textsuperscript{10} postulated that diabetes, hypertension and obesity were independent risk factors for the development of endometrial polyps, but statistical analysis of all the independent variables (odds ratio [OR] 1.05, 95% confidence interval [CI] 1.02–1.07, \( P < 0.001 \)) showed that only increasing patient age was a significant risk factor and that it acted as a confounder for all the postulated risk factors.

When looking for predictors of malignancy or premalignancy in endometrial polyps, Wang \textit{et al.}\textsuperscript{11} observed that a size of \( > 10 \) mm (OR 2.93, 95% CI 1.19–7.20), postmenopausal status (OR 4.85, 95% CI 2.09–11.27) and abnormal uterine bleeding (OR 3.97, 95% CI 1.71–9.18) were all independent risk factors (\( P < 0.05 \)). In addition, vaginal bleeding increased the malignant potential of endometrial polyps by a factor of 10 compared with asymptomatic women, as shown in a study of 922 postmenopausal women.\textsuperscript{12} Wang \textit{et al.} also reported that a polyp diameter of \( > 18 \) mm in asymptomatic women increased the risk of malignancy (OR 6.9, CI 2.2–21.4), which was otherwise very low. Further studies are required to ascertain whether incidental endometrial polyps of \( < 18 \) mm in asymptomatic postmenopausal women can be safely treated conservatively. However, there is a higher incidence of concurrent endometrial hyperplasia with endometrial polyps, especially in women on hormone replacement,\textsuperscript{13,14} which should also be taken into account in the management plan.

Malignant endometrial polyps

A systematic review of endometrial polyp studies\textsuperscript{16} pooled data from 46 studies which included 9266 pre- and postmenopausal symptomatic and asymptomatic women with endometrial polyps. Most studies were retrospective and showed large variation due to a heterogeneous case mix regarding patient age and symptoms. The prevalence of atypia and malignancy was 0.8% and 3.1%, respectively. Hysteroscopic markers for malignant endometrial polyps include surface irregularities such as necrosis, vascular irregularities and whitish thickened areas, which are indications for obtaining a histological diagnosis.\textsuperscript{17} Mittal \textit{et al.}\textsuperscript{18} recommend hysterectomy once the diagnosis of complex atypical hyperplasia or carcinoma in situ in endometrial polyps is made, due to their findings that of 29 women with complex atypical hyperplasia within a polyp, 19 were found to have hyperplasia of the non-polyp endometrium and nine had uterine adenocarcinoma. Of the eight women with adenocarcinoma in situ in the endometrial polyp, three had myoinvasive adenocarcinoma. In contrast, Scrimin \textit{et al.}\textsuperscript{19} report that after resectoscopic polypectomy of focal atypia in postmenopausal high-anaesthetic-risk women (\( n = 16 \)), all the women remained disease-free after 5 years. Larger prospective studies are needed to determine the optimal treatment.

Endometrial polyps and fertility

In the reproductive age group, large or multiple endometrial polyps can contribute to infertility and increase the risk of miscarriage. Pérez-Medina \textit{et al.}\textsuperscript{20} randomised 215 infertile women with ultrasonographically diagnosed endometrial polyps, prior to intrauterine insemination, to hysteroscopic polypectomy or polyp biopsy only. Women had a better chance of becoming pregnant after polypectomy (relative risk [RR] 2.1, 95% CI 1.5–2.9) than after biopsy. In women in whom the only reason for subfertility was endometrial polyps, Stamatellos \textit{et al.}\textsuperscript{21} showed that hysteroscopic polypectomy improved the rate of spontaneous conception regardless of size or number of polyps, which may be due to the normalisation of endometrial implantation factors.\textsuperscript{22}

Diagnostic modalities

Endometrial polyps can be diagnosed with ultrasound, saline infusion sonogram or hysteroscopy, which is the gold standard. Saline infusion sonogram (SIS), which uses a sterile normal saline solution to distend the endometrial cavity and outline polyps, is a highly sensitive, well-tolerated, safe, rapid and minimally invasive\textsuperscript{23} diagnostic technique. It is superior to transvaginal ultrasound scanning (TV USS) when diagnosing endometrial polyps: the likelihood ratios for a positive result are 2.7 for TV USS and 15.5 for SIS. The likelihood ratios for a negative result are 0.46 for TV USS and 0.07 for SIS.\textsuperscript{24} Only hysteroscopy, however, allows for concurrent treatment.

Treatment of endometrial polyps

Although the risk of malignant transformation is low, endometrial polyps should be removed when detected, as excision allows for both histological diagnosis and effective treatment of abnormal uterine bleeding patterns and excessive menstrual loss; in addition, endometrial polyps in postmenopausal women are more likely to be malignant when symptomatic.\textsuperscript{12}

The question arises whether asymptomatic and incidental endometrial polyps should be treated. DeWaay \textit{et al.}\textsuperscript{5} observed natural regression of over half of endometrial polyps \(< 1 \) cm in asymptomatic premenopausal women who underwent SIS with a 2.5 year follow-up, whereas larger endometrial polyps tended to become symptomatic. Similarly, Haimov-Kochman \textit{et al.}\textsuperscript{25} reported a small case series of asymptomatic women diagnosed with endometrial polyps of 5–8 mm on hysteroscopy, which regressed after several months.

In the absence of a randomised trial, it is current practice to remove all endometrial polyps in asymptomatic postmenopausal women. Retrospective reports are conflicting: Domingues \textit{et al.}\textsuperscript{26} found no cases of cancer in a subgroup of postmenopausal women with asymptomatic endometrial
polyps \((n = 89)\), but Lieng et al.\(^{27}\) reported that two out of 74 women with asymptomatic endometrial polyps had malignancy/atypical hyperplasia (CI 0.7–10.4). Unfortunately, a much needed prospective study on conservative endometrial polyp treatment in postmenopausal women was abandoned due to poor recruitment.\(^{28}\)

Figure 1 shows a suggested treatment algorithm.

**Hysteroscopic resection**

Most endometrial polyps are blindly avulsed or removed by curettage and the cavity hysteroscopically inspected before and after, but not during, avulsion.\(^{29}\) Uterine bleeding often obscures the second look. However, there is good direct and circumstantial evidence that hysteroscopic resection of endometrial polyps under vision is safe, simple and superior to blind techniques:

- Malignant cells at the base of the polyp can be missed with blind avulsion.\(^{30}\)
- Hysteroscopic resection avoids excessive cervical dilatation, which is when uterine perforation and creation of a false passage usually occur.\(^{31}\)
- Not a single recurrence of endometrial polyps was reported when resection under vision was compared with removal with a grasping forceps (recurrence rate 15%).\(^{32}\)

Resection is feasible even in an outpatient setting without general anaesthesia, which has become possible due to small-diameter instruments, which obviate the need for cervical dilatation. See-and-treat outpatient hysteroscopy is cheaper than inpatient hysteroscopy under general anaesthesia (€686 and £779, respectively)\(^{33}\) but as acceptable to women and with faster recovery.\(^{34}\) Recruitment is under way for a multicentre study funded by the Department of Health: the OPT (Outpatient Polyp Treatment) Trial (see Websites section). The aim is to recruit 480 women and to compare the cost and acceptability of outpatient versus inpatient hysteroscopic endometrial polyps removal.

At The Royal London Hospital endometrial polyps are routinely resected in the outpatient hysteroscopy unit. Patient discomfort is minimised by using suggestions from Clark et al.\(^{35}\) The procedure is carried out as follows:

- Non-steroidal anti-inflammatories or tramadol are given orally 1 hour prior to the procedure, which can be carried out at any time during the cycle unless the woman is bleeding heavily, without the need for routine antibiotic cover.
- With the woman in the lithotomy position and a staff member providing one-to-one attention, vaginoscopy is carried out.
- A Gynecare Versascope\(^{\text{TM}}\) (ETHICON\(^{\text{TM}}\) Women’s Health & Urology UK) hysteroscopy system (Figure 2), consisting of an Alphascope\(^{\text{TM}}\) (1.9 mm) and a sheath with a 3.5 mm expandable operating channel is inserted into the posterior vaginal fornix under normal saline irrigation.
- The cervix is then ‘loaded’ onto the hysteroscope and during gentle withdrawal of the hysteroscope the cervical canal moves into the field of vision. After allowing time for cervical hydrodilatation the scope is gently navigated through the cervical canal with minimal lateral movement and tissue contact.
- Once the endometrial polyp is visualised the hysteroscope is adjusted by moving the sheath to allow good access to the endometrial polyp base from the operating channel.
- In The Royal London Hospital hysteroscopy outpatient department, most endometrial polyps are resected with cold scissors down to a thin stalk and then retrieved under
vision with a hysteroscopic grasper. Bipolar electrosurgical resection with bipolar twizzles (Figure 2)\(^{36}\) and polyp snare (Figure 3)\(^{37}\) also show good success and low pain scores.

- Polyps >2 cm require piecemeal removal, a longer operating time and multiple instrument passes through the cervix. In those cases we recommend removal under general anaesthesia, but small-diameter hysteroscopic morcellators are becoming available for this indication (see Figure 4 and Movie S1, a video of the TRUCLEAR\textsuperscript{TM} hysteroscopic morcellator in use).

There is good evidence that outpatient hysterectomy is safe,\(^{38}\) feasible and has similar outcomes when compared with polypectomy under general anaesthesia.\(^{39}\) The vaginoscopic approach to hysteroscopy causes less pain than the traditional approach using a speculum and tenaculum\(^{40}\) but is similarly successful in achieving polypectomy.\(^{41}\)

Failure of outpatient hysterectomy is attributable to technical difficulty due to anatomical factors, including cervical stenosis, inadequate visualisation and patient tolerance.\(^{38}\) It is important to stress that outpatient hysterectomy is acceptable to most women\(^{42}\) and that, on average, it is considered less painful than menstruation.\(^{34}\)

**Conclusion**

Endometrial polyps are a common finding in gynaecology. Their generally low malignant potential increases with endometrial polyp size, symptoms and patient age. These factors need to be taken into account when considering treatment options (Figure 1). Incidental small endometrial polyps in premenopausal women may be amenable to conservative treatment due to their low malignant potential and chances of regression. However, endometrial polyps that lead to infertility, postmenopausal bleeding, menorrhagia and abnormal bleeding patterns and those in postmenopausal

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**Figure 2.** Gynecare Alphascope hysteroscopy system (reproduced with permission from ETHICON\textsuperscript{TM} Women’s Health & Urology UK), consisting of a 0-degree hysteroscope (bottom) and a single-use sheath (top), containing in and outflow tubing and an expandable operating channel.

**Figure 3.** Hysteroscopy polyp snare. The loop is placed around the base of the polyp and closed. A current is applied and the endometrial polyp cut at the base. The loop is then used to grip the polyp, which is subsequently removed under vision, together with the hysteroscope. Image courtesy of Cook Medical Inc.

**Figure 4.** The TRUCLEAR\textsuperscript{TM} 5 mm 0-degree hysteroscopic morcellator simultaneously resects and aspirates endometrial polyps and small fibroids. (Reproduced courtesy of Smith & Nephew)
women warrant hysteroscopic removal under vision, which is superior to blind avulsion. Adequate patient selection, psychological support, a competent operator and a setting that creates a private, caring and calm environment are prerequisites for carrying out this procedure in the outpatient setting. Future studies are required to determine the role of skin disinfection and the optimum distension pressure.

**Websites**

The OPT Trial [www.opt.bham.ac.uk/investigations/]

**Supporting information**

The following supplementary information is available for this article online:

**Movie S1.** The 5 mm 0-degree hysteroscopic morcellator in use. Reproduced courtesy of Smith & Nephew.

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