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ORIGINAL ARTICLE

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Long-term impact and risk factors for hysterectomy after hysteroscopic surgery for menorrhagia

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Abstract The objective of this study was to assess the long-term impact of management and establish the incidence of hysterectomy, and to identify factors predictive of failure of the procedure among women who had undergone hysteroscopic endometrial resection with or without myomectomy for menorrhagia. Clinical history and data on additional treatment and follow-up status were obtained by medical record review and postal questionnaire for 279 women who had undergone hysteroscopic surgery. Follow-up data were available for 259 (93%) cases, and the mean follow-up was 6.0 years. Subsequent hysterectomy was the primary endpoint, and its incidence was calculated by survival analysis. Univariant analysis and Cox regression model were used to identify predictors of failure. Myomas, polyps, adenomyosis, or endometrial hyperplasia were found in 40.9% of hysteroscopic procedures. Perioperative complications occurred in 5.7% and late complications in 7.7%. During the follow-up period, 97 (37.5%) of 259 women underwent at least one gynecological procedure. The incidence of hysterectomy was 23.6% (95% confidence interval: 18.8–29.1%). Positive predictive factors for hysterectomy were long uterine cavity (≥9 cm) and tubal ligation. Most (82.8%) of the 198 women who did not undergo hysterectomy had postoperative oligo- or amenorrhea. Hormone replacement therapy was common (67%) among postmenopausal women after endometrial resection. Hysteroscopic resection of the endometrium and concomitant hysteroscopic resection of fibroids for the treatment of menorrhagia is a suitable alternative to hysterectomy and offers lasting results. A large uterine cavity indicating possible uterine pathology and tubal ligation associated with hematometra increase the risk of hysterectomy.

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Introduction

Hysteroscopic surgery, including endometrial resection, myomectomy, and polypectomy, is an accepted alternative to hysterectomy in the treatment of menorrhagia [1–3]. Several transcervical endometrial ablation methods have been used for the purpose. The first-generation hysteroscopic procedure is performed using electrical energy for endometrial resection with loop or endometrial coagulation with rollerball or the endometrium is destroyed with laser energy [1, 2]. The second-generation methods are mostly non-hysteroscopic techniques using different sources of energy to destroy the endometrium [1, 2]. Hysteroscopic resection of the endometrium is one of the oldest, often combined with myomectomy or polypectomy, which is a great advantage of this technique [1, 2, 4]. Operative outcomes, perioperative complications, and short-term follow-up results are well documented [2–4]. However, long-term results of endometrial resection are sometimes less striking than those in the immediate postoperative period. The long-term impact and factors prognostic for subsequent hysterectomy are not well known. In addition, hormonal replacement therapy in women who have reached menopause after endometrial ablation has not been extensively studied.

Our aim was to evaluate long-term outcomes and hysterectomy rates after endometrial resection for menorrhagia and to identify factors predictive of hysterectomy in these patients.

Patients and methods

Between November 1990 and May 1999, 279 consecutive women underwent hysteroscopic endometrial resection with or without concomitant myomectomy at the Department of Obstetrics and Gynecology in the University

Hospital of Tampere, Finland. The mean age of the patients was 42 years (range: 15–68 years); 171 (61.3 %) were between 40 and 49 years, and 18 (6.5%) women were postmenopausal and menorrhagia was linked to hormone replacement therapy. Mean body mass index (BMI) (SD) was 25.9 (4.8) kg/m^2. Mean parity was 2.0 (range: 0–5) and 29 (10.4%) had undergone cesarean section. Tubal ligation for sterilization had been performed in 141 (50.5%) cases.

All patients suffered from menorrhagia and were candidates for hysterectomy. One hundred and eighty (64.5%) women had previously received medical therapy for menorrhagia, most frequently oral cyclical or continuous progestogen (34.1%), tranexamic acid (28.0%), or a levonorgestrel-releasing intrauterine system (17.9%). Fifty-two (18.6%) patients were treated hysteroscopically for a medical disorder constituting a significant risk at hysterectomy. Seventeen had heart disease, 8 were receiving anticoagulant therapy, 12 were mentally retarded, 8 had a neurological disease, 7 a nongynecological malignancy, and 8 kidney or other disease. Five women had severe obesity (BMI 40–53 kg/m^2).

Cervical smear and endometrial biopsy were taken preoperatively. Transvaginal ultrasonography was employed to determine the size and location of possible myomas or endometrial polyps. Women with a uterus larger than the size of a 12-week pregnancy were excluded from the study, but isolated submucous fibroids less than 5 cm in diameter were not an exclusion criterion. Women with endometrial hyperplasia, uterovaginal prolapse, untreated adnexal disease, or acute pelvic inflammatory disease were excluded from resection. Women desiring future pregnancy were also excluded.

Preoperative endometrial suppression with hormonal therapy was used in 100 cases (35.8%). The treatment consisted of danazol, gonadotropin-releasing hormone (GnRH) agonist (goserelin), or continuous progestogen treatment with a levonorgestrel-releasing intrauterine system or continuous oral progestogen therapy (lynesterol). In other cases surgery was performed on days 4–9 of the menstrual cycle.

The procedure was carried out under spinal anesthesia in 136 cases (48.7%). The uterine cavity was distended with 2.2% isotonic glycine (Baxter Health Care Ltd., Thetford, UK) and the endometrium was resected using a 26 French resectoscope as previously described [5]. Antibiotic prophylaxis was given when appropriate. Sixty-eight women (24.4%) had concomitant hysteroscopic myomectomy and 42 (15.1%) laparoscopic tubal ligation.

The length of the uterine cavity was measured prior to the hysteroscopic procedure using uterine sounding. The mean (SD) length of the uterine cavity was 8.7 (1.0) cm and ranged from 6.5 cm to 13.0 cm. A cavity 9 cm or more in length was regarded as large.

Hospital records of the patients were examined for details of preoperative history, operative procedures, further surgical treatment, and documented follow-up. Patients who had not undergone hysterectomy during the follow-up period were sent a postal questionnaire to assess long-term effects. Questions concerned the need for further treatment, hormonal treatment, bleeding patterns, and success of treatment. Respondents were asked whether they had amenorrhea, slight menstruation for 1–3 days, slight menstruation for 4–6 days, or no improvement in menstrual flow or increased menstrual flow.

Follow-up data were received from 259 patients (92.8%). Five had died and 15 were lost to follow-up. The mean follow-up period was 6.0 years (range: 0.3–11.0 years).

Statistical analysis was made using the SPSS for Windows, version SPSS 11.5 (SPSS Inc., Chicago, IL, USA). Subsequent hysterectomy was the primary endpoint and its incidence was calculated by survival analysis (Kaplan-Meier). The association between hysterectomy and possible factors was tested by univariant analysis. A multivariant analysis was then made using the Cox regression model with backward stepwise method to identify the subset of variables most accurately predictive of the risk of hysterectomy. The level of significance was set at $p<0.05$.

Results

Operative complications were recorded in 16 (5.7%) of 279 operations. Uterine perforation occurred in two women (0.7%). The first had cervical perforation during the cervical dilatation at commencement of surgery and endometrial resection was not undertaken. This patient had previously received intracavitary radiation therapy for menorrhagia. The second sustained uterine perforation and disruption of the uterine artery in connection with myomectomy, requiring emergency hysterectomy. Excess bleeding was controlled by tamponade using a Foley catheter placed in the endometrial cavity in six cases (2.2%). Eight women (2.9%) with postoperative endometritis recovered completely after antibiotic treatment. Glycine deficit during the operation was over 1 l (range: 1.0–1.8 l) in only eight patients (2.9%), but none of these developed hyponatremia. Of 136 women with spinal anesthesia, 13 (9.6%) suffered from postspinal headache, which was successfully treated with a blood patch.

At least one abnormal finding in endometrial specimens was reported in 114 (40.9%) cases. Concomitant hysteroscopic resection of fibroids was performed in 68 (24.4%) and polypectomy in 25 (9.0%). The mean size of the fibroids was 2.0 cm (range: 0.5–5.0 cm). Adenomyosis was detected in 21 specimens (7.5%). Despite earlier endometrial biopsy seven (2.7%) women were found to have endometrial hyperplasia without atypia.

Late complications occurred in 20 (7.7%) of 259 women with follow-up. Hematometra developed in 18 (6.9%) cases and 14 of these had undergone tubal ligation. Two pregnancies (0.8%) occurred after endometrial resection, one having induced abortion during the first trimester 6 months postoperatively and the other a spontaneous miscarriage with placenta accreta with subsequent hysterectomy.

During the follow-up, 97 (37.5%) of 259 women underwent at least one gynecological procedure (Table 1). Endometrial ablation was repeated because of hematometra, spotting bleeding, or request for amenorrhea. Hysterectomy was performed in 61 cases [23.6%, 95% confidence interval (CI): 18.8–29.1%]. The main indications for subsequent hysterectomy applied to 21 cases with myomas, 13 adenomyosis, 11 persistent menorrhagia or endometrial hyperplasia, 7 peri- or postoperative complications (uterine perforation, pregnancy, hematometra), 8 endometriosis or genital prolapse, and 1 case with unknown reason. Malignancy was not found in any case. Survival analysis shows a relationship between the probability of not undergoing subsequent hysterectomy and the time since the endometrial ablation procedure (Fig. 1). Most (83.6%) of the hysterectomies were performed during the first 5 years after the hysteroscopic surgery.

Table 2 shows the results of univariant analysis and the Cox regression model.

A history of tubal ligation and length of uterine cavity 9 cm or more were associated with an increased risk of hysterectomy in both univariant and multivariant analysis. Perioperative complication was a significant factor in univariant but not in multivariant analysis (Table 2).

Long-term follow-up data were available for 198 women who did not require hysterectomy. One hundred women (50.5%) reported amenorrhea, 64 (32.3%) had slight bleeding for 1–3 days, and 24 (12.1%) had slight bleeding for 4–6 days. Ten women (5.1%) estimated that their bleeding had become scantier than before the hysteroscopic procedure.

Of 198 women, 112 (56.6%) had reached menopause during the follow-up period; 75 of them (67.0%) used hormonal replacement therapy, 30 used a continuous combined estrogen and progestogen regimen or tibolone, 38 a cyclical combined regimen, 4 reported using only estrogen, and 3 had only a cyclical progestogen regimen. Of 38 women on a cyclical combined estrogen and progestogen regimen, 19 (52.6%) reported that they were amenorrheic.

Discussion

Hysterectomy was the primary endpoint in this study, as a hysteroscopic procedure was undertaken mostly instead of hysterectomy in women suffering from menorrhagia. The rate of hysterectomy after endometrial resection was 23.6% in the present study and 15–24% in previous studies with a follow-up period of 4 years or more [6–8]. The indication for uterine removal was in most cases uterine fibroids or adenomyosis. Our study also included cases undergoing hysterectomy with no relationship to endometrial resection, for example endometriosis or uterine prolapse. It is evident that a long follow-up period makes it possible to develop many diseases of the uterus which are not related to the treatment of menorrhagia. These patients therefore need follow-up years after hysteroscopic treatment.

Hysterectomies were performed mostly during the first 5 years after hysteroscopic surgery. Those women who had amenorrhea or hypomenorrhea after hysteroscopic surgery also maintained this response years after treatment. This technique did not merely postpone hysterectomy as three of four women had a permanent result.

Both univariant and multivariant analysis showed that a length of the uterine cavity of 9 cm or more was a significant risk factor for hysterectomy. A long uterine cavity may be associated with a large uterine cavity, when the endometrial surface to resect is larger and liable to incomplete resection [2, 9]. In addition, the uterine cavity may be insufficiently expanded preventing complete resection. Furthermore, menorrhagia and a long uterine cavity may be associated with other uterine pathology such as adenomyosis or uterine fibroids. Neis and Brandner [10] reported that women with dysmenorrhea and a uterine cavity over 10 cm show a high incidence of adenomyosis. They run an increased risk of failure and should be excluded from endometrial ablation [10]. Submucous

Table 1 Further treatment after hysteroscopic management of menorrhagia in 259 patients during the follow-up

Treatment	Number of patients (%)
Any further treatment	97 (37.5)
Hysterectomy	61 (23.6)
Endometrial reablation	20 (7.7)
Hysteroscopy, curettage	18 (6.9)
Cervical dilatation and drainage	9 (3.5)
Salpingo-oophorectomy	6 (2.2)
Continuous progestin	3 (1.2)

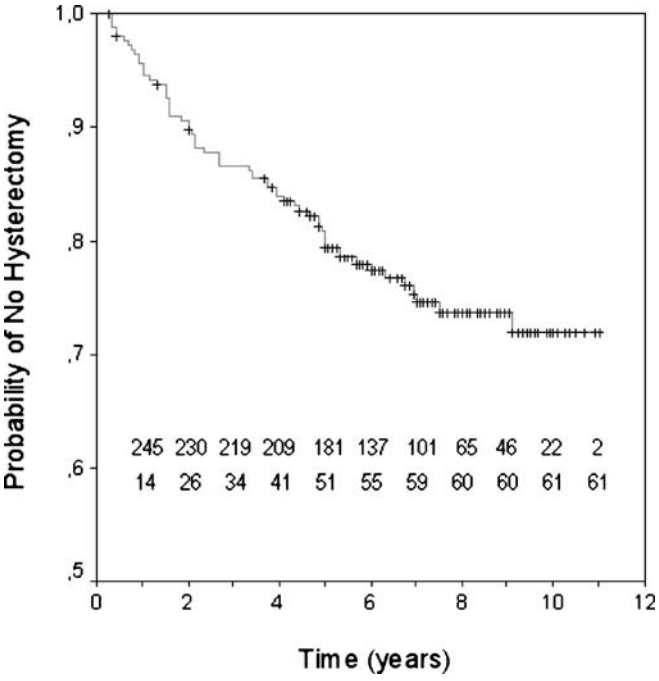

Fig. 1 Probability of not having a hysterectomy (Kaplan-Meier curve). The *upper figure line* indicates the number of cases in follow-up and the *lower line* the cumulative number of cases with hysterectomy

Table 2 Predictors of hysterectomy in patients with hysteroscopic surgery for menorrhagia

Predictor[a]	Univariant analysis			Cox regression model		
	Hazard rate ratio	95% CI	*p*	Hazard rate ratio	95% CI	*p*
Tubal ligation	4.15	2.36–7.27	0.020	1.954	1.048–3.643	0.035
Perioperative complication	2.06	1.10–3.,88	0.049	2.088	0.854–5.106	0.106
Length of uterine cavity ≥9 cm	1.87	1.19–2.94	0.005	1.993	1.187–3.347	0.009

[a]The following items were not statistically significant: age, medical disease, cesarean delivery, endometrial thinning, use of levonorgestrel-releasing intrauterine system, late complication, abnormal histology, adenomyosis, myomectomy

fibroids were the most common pathology needing additional treatment with endometrial resection. Only this kind of myoma was possible to resect, intramural myomas being impossible to treat although they may enlarge the uterus [9].

A significant number (13%) of women after endometrial resection have patent fallopian tubes [11]. Contraception is necessary after endometrial resection, since pregnancy is possible, as two cases in the present study demonstrated. Tubal ligation, which was also a risk factor for hysterectomy, was the most common method of contraception. An association between hematometra, endometrial resection, and tubal ligation has previously been reported [12]. Patent fallopian tubes may allow egress of blood and prevent the formation of hematometra. Most cases with painful hematometra can be treated by transcervical drainage. The definitive treatment is resectoscopic diathermy to residual areas of the endometrium [12]. However, this treatment is not always successful and hysterectomy may be necessary.

About half of the women without hysterectomy had reached menopause during a long follow-up period, and many of them (67%) were on hormone replacement therapy (HRT). Combined treatment with estrogen and progestogen was the most popular as it does not cause endometrial proliferation. Almost half of the postmenopausal women on cyclic estrogen and progestogen regimen had amenorrhea, showing good results after endometrial resection. Unopposed estrogen treatment is not recommended after endometrial ablation even where a woman has amenorrhea after endometrial resection. Endometrial cells are found in endometrial samples in women with amenorrhea after endometrial resection [13]. Istre and associates reported endometrial hyperplasia in women on an unopposed estrogen regimen [14]. Those receiving a continuous combined estrogen and progestogen regimen had no endometrial hyperplasia. Women who have undergone endometrial resection must follow the same guidelines during HRT for endometrial protection as women with an intact uterus [14]. Postmenopausal women after endometrial resection and receiving HRT should undergo measurement of endometrial thickness using transvaginal ultrasound at follow-up examinations. Those with postmenopausal bleeding should be checked by endometrial biopsy, as endometrial carcinoma has been reported after endometrial resection [15].

Nowadays endometrial resection has been replaced by second- and third-generation endometrial ablation techniques [16]. However, submucous and pedunculated intracavitary fibroids and endometrial polyps are treated by the resection technique [2, 3]. Submucous myomas and polyps were the most common findings in this as in previous studies [17]. The combination of resection of fibroids or polyps prior to endometrial ablative technology may be one possible way to treat these patients.

Hormonal treatment with a levonorgestrel-releasing intrauterine system has been reported as an alternative to hysterectomy in women with heavy menstrual bleeding [18]. Studies comparing intrauterine hormonal treatment and endometrial resection have given similar results for the 12-month follow-up period [19, 20]. In the present study 50 (17.9%) women had used a levonorgestrel-releasing intrauterine system prior to endometrial resection. Hysteroscopic surgery may also be an effective mode of therapy in women who have not been satisfied using a levonorgestrel-releasing intrauterine system to treat menorrhagia instead of hysterectomy.

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