

# Retrospective Cohort Study on the Symptomatic Recurrence Pattern after Hysteroscopic Polypectomy

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## Abstract

**Objectives:** The recurrence rate of benign endometrial polyps after a hysteroscopic polypectomy is low, between 0% and 15%. There are limited follow-up duration data on recurrence factors for benign polyps after hysteroscopic polypectomy, including recurrences with Versapoint® versus resectoscope. This study aims to estimate the rate of symptomatic recurrence following hysteroscopic polypectomy and to analyze the possible risk factors involved with Versapoint® versus resectoscope.

**Materials and Methods:** We designed a retrospective cohort study in a tertiary university hospital in Seville (Spain) which looked at the results of polypectomy with a 9-mm resectoscope on 42 women between 2008 and 2015 compared to 151 women using Versapoint® during 2014.

**Results:** The rate of first recurrence was 24.35%. There was a strong positive correlation between the recurrence and the follow-up duration (odds ratio [OR] = 2.58; 95% confidence interval [CI] = 1.68–5.04;  $P = 0.000$ ), the polyps causing abnormal uterine bleeding (OR = 2.5; 95% CI: 1.1–3;  $P = 0.04$ ), and a polyp size >15 mm (OR = 1.63; 95% CI = 1.3–3.1;  $P = 0.02$ ). There were no statistical differences in polyps' recurrence among the types of hysteroscopic polypectomy ( $P > 0.05$ ).

**Conclusion:** The main risk factors for recurrence were polyps causing abnormal uterine bleeding, size, and follow-up duration.

**Keywords:** Endometrium, hysteroscopy, polyp, recurrence, risk factors

## INTRODUCTION

The recurrence of an endometrial polyp is defined by two criteria: same type of histology and same location. Given that hysteroscopy allows for the resection of polyps, the recurrence rate is low (0%–15%).<sup>[1]</sup>

There are limited follow-up duration data on recurrence factors for polyps after hysteroscopic polypectomy,<sup>[2-4]</sup> including recurrences with Versapoint® versus resectoscope, and there is controversial about the risk factors for recurrence. The objective of the study is to calculate the polyps' recurrence rate after hysteroscopic polypectomy, regarding the type of polypectomy. We also sought to

investigate other recurrence risk factors independent of the type of polypectomy.

## MATERIALS AND METHODS

### Participants

We included 193 women who met the inclusion criteria in a retrospective cohort study. The sample was composed of 42 cases of resectoscopic polypectomy under anesthesia in the period 2008–2015 and 151 polypectomies performed in 2014 using the Gynecare Versapoint™ (Ethicon, Blu Ash, USA) bipolar electrode at the hysteroscopy unit

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office, at a tertiary university hospital in Seville, Spain. The presence of an endometrial polyp was confirmed with histology. The inclusion criteria were as follows: women diagnosed histologically of an endometrial polyp treated with hysteroscopy; data regarding the histologic type, the location of the polyp, and the free-disease interval after polypectomy were found in their symptomatic history.

The exclusion criteria were previous endometrial resection or ablation after polypectomy and any form of diffused endometrial hyperplasia.

The tests we performed to define recurrence were an endovaginal ultrasound scan, and in case of polyp suspicion, we performed an office hysteroscopy. The recurrence of an endometrial polyp is defined by two criteria: same type of histology and same location, which differentiates it from a new polyp.

There were not defined follow-up duration intervals after polypectomy since we captured those women who consulted for symptoms after hysteroscopic polypectomy.

The outcome variables in research were age, parity, body mass index (BMI), high blood pressure, diabetes mellitus, chronic anovulation, endometriosis, estrogen used without progestogen, use of tamoxifen, menopausal status, hypothyroidism under treatment with levothyroxine, symptomatology, number of polyps, polyp's histological type, polyp's size, location of polyps, type of hysteroscopic polypectomy, follow-up duration (disease-free interval until symptomatic recurrence), and presence of a new polyp.

The data source was the electronic medical records of the patients. The participants signed a consent statement of ethical approval to use their data.

## Procedure

Patients who underwent hysteroscopy since 2012 took 600 mg ibuprofen and 5 mg diazepam, taken orally 30 min to 1 h beforehand. Routine hormonal contraceptives were not given to premenopausal women nor local anesthetic was administered. The protocol does not consider the limit of the polyp's size, indicating polypectomy with Versapoint® or resectoscope.

The hysteroscopy was carried out with a rigid and continuous-flow Bettocchi hysteroscope (Karl Storz Endoskope, Tuttlingen, Germany) of 2.9 mm, with a 30-degree angled lens, and a 5 Fr working channel. A sodium chloride saline solution at 0.9% was used for uterine distension. The level of intrauterine pressure given by a pump was 80–100 mmHg and the liquid balance was controlled in every case. The removal of the polyps was carried out with Versapoint® (VC3; 18 W) and crocodile forceps. The hysteroscopy in the operating

theater was performed under sedation or intradural anesthetic. It was carried out with a 9-mm resectoscope, a 30-degree scope, and a semicircular 90-degree diathermy loop. Monopolar cut was set at 60–80 W using glycine at 1.5%, and if a bipolar loop was chosen, we used cut at 60–80 W and a sodium chloride saline solution at 0.9%. A pressure pump was used at 100mmHg controlling the liquid balance. The polyps' size was measured using a transvaginal ultrasound and confirmed by a hysteroscopy and the pathological analysis. The polyp's type was determined by histological analysis.

## Statistical analysis

We calculated the sample size with the G\*Power 3.0 software (Heinrich Heine Düsseldorf University, Germany) ( $\alpha = 0.05$ ; power = 0.80; large effect size). The result of a statistical estimation of the appropriate sample size was 197 women. Four hundred and eleven women who underwent a hysteroscopic polypectomy in 2010–2015 were potentially eligible. IBM SPSS Statistics for Windows, version 22 (Armonk, NY, USA: IBM Corp.) was used.

The results were expressed in absolute numbers and percentages for discrete variables and average  $\pm$  standard deviation for continuous variables. The normality tests used were Kolmogorov–Smirnov when the degree of freedom was higher than 50 and Shapiro–Wilk test when the degree of freedom was  $<50$ . The Mann–Whitney U/Wilcoxon test was used to contrast the hypothesis of the ordinal and continuous variables. The Chi-square test was used for qualitative variables. The Fisher's exact test was used to contrast between the dichotomy variables, the Spearman's test to study the correlation between quantitative variables using normal distribution, and the log rank (Mantel–Cox test) to contrast the survival of two populations.

A  $P < 0.05$  (95% confidence interval, [CI]) was considered statistically significant.

The study has been approved by the institutional ethics committee (reference no. 28818216K).

## RESULTS

First, we performed a descriptive and a statistical analysis of the variables for the polypectomy type to determine whether both groups were homogeneous in order to investigate polyps' recurrence according to the type of hysteroscopic polypectomy. We concluded that there was no significant statistical difference between the variables studied for the type of polypectomy ( $P > 0.05$ ), except in terms of menopausal status ( $P = 0.04$ ) and the size of the polyp ( $P = 0.001$ ). We could not study statistically if there were differences in terms of hysteroscopist's expertise according to the type of

hysteroscopic polypectomy. As these previous factors can be confounding factors, we could not study whether there were significant statistical differences in recurrence, according to the type of hysteroscopic polypectomy.

The average age was  $49.4 \pm 12.45$  years (95% CI = 46.43–52.33). The majority of women (60; 31.08%) were aged 36–45 years, and 45 (23.32%) women were aged 46–55 years. 33 (16.93%) women were 25–35 years of age, 29 (15.02%) women were 56–65 years of age, and 26 (13.47%) women were older than 65 years of age. The median of parity was two births (95% CI = 1.59–2.36; range = 0–8) and 36 (18.5%) were nulliparous. A Spearman's test found that age and parity were not correlated with a high risk of recurrence after polypectomy ( $P = 0.11$  and  $P = 0.175$ , respectively; odds ratio [OR] = 1).

There were 12 (6.22%) women treated with tamoxifen 20 mg per day, and there was no association between the use of tamoxifen and recurrence ( $P = 0.61$ ). In regard to polyp size in the Versapoint® group, 78% of the procedures were performed in a single surgery and 22% in two separate surgeries. A strong positive association existed between the variables, polyp size  $\geq 15$  mm and recurrence (OR = 1.63; 95% CI = 1.3–3.1;  $P = 0.02$ ). The first recurrence was in the Versapoint® group, which occurred at an average of  $22 \pm 17.80$  months (42 cases; 21.76%) and at an average of  $2.5 \pm 28.60$  months with resectoscope (11 cases; 5.69%). The average follow-up duration was  $32.27 \pm 21.85$  months (95% CI = 27.44–37.87). The follow-up duration after the polypectomy is shown in Table 1. The follow-up duration range was 2–96 months, and a positive correlation was found between follow-up duration and recurrence: <1 year (OR = 0.57); 1–2 years (OR = 0.24); and >3 years (OR = 2.58; 99% CI = 1.68–50.04;  $P = 0.000$ ). A strong positive association was found between long-term follow-up duration for more than 3 years and recurrence; however, the type of polypectomy did not influence the follow-up duration until the appearance of the first recurrence ( $P = 0.206$ ; log rank test).

Regarding the hysteroscopist's expertise, 18 (9.33%) hysteroscopic polypectomies (3 Versapoint® + 15 resectoscopies) were carried out by an internal medicine resident supervised by an expert hysteroscopist surgeon, 19 (9.84%) procedures

(10 Versapoint® + 9 resectoscopies) were carried out by a nonexpert hysteroscopist surgeon, and finally, 156 (80.83%) procedures were carried out by an expert hysteroscopist surgeon (138 Versapoint® + 42 resectoscopies).

Within the population studied were 48 cases with high blood pressure (24.87%); there was no association between high blood pressure and recurrence ( $P = 0.06$ ). When analyzing the obesity variable, 151 women (78.20%) had a normal weight, 23 (11.90%) had obesity Grade I (BMI = 30.0–34.9 kg/m<sup>2</sup>), 8 (4.20%) obesity Grade II (BMI = 35.0–39.9 kg/m<sup>2</sup>), and 11 (5.70%) obesity Grade III (BMI  $\geq 40.0$  kg/m<sup>2</sup>). Using the Chi-square test, we found a significant statistical difference between the degree of obesity and a higher number of polyps ( $P = 0.01$ ); however, the association between obesity and recurrence was negative (OR = 0.35;  $P = 0.06$ ). Regarding the diabetes variable, we found 14 women with diabetes (7.25%) without significant statistical differences between diabetes and recurrence ( $P = 0.64$ ). Some 30 (15.54%) women had hypothyroidism under treatment with levothyroxine, and there was no association between the hypothyroidism variable and recurrence ( $P = 0.82$ ). In no case, estrogen without progestogen was used. Only one of the women had chronic anovulation (0.52%). Three women suffered from endometriosis (1.55%) without an association with recurrence using Mann–Whitney *U*-test ( $P = 0.31$ ).

With regard to menopausal status, 122 (63.21%) women were premenopausal and 71 (36.79%) postmenopausal. We did not find association between recurrence and menopause ( $P = 0.13$ ).

The symptomatology of participants affected by endometrial polyps was uterine abnormal uterine bleeding (AUB) (128, 67%), sterility (13, 7%), and dysmenorrhea (9, 5%). 40 (21%) participants were asymptomatic. The symptomatology, especially AUB, had a strong positive association with relapse (OR = 2.25; 95% CI = 1.1–30.0;  $P = 0.046$ ).

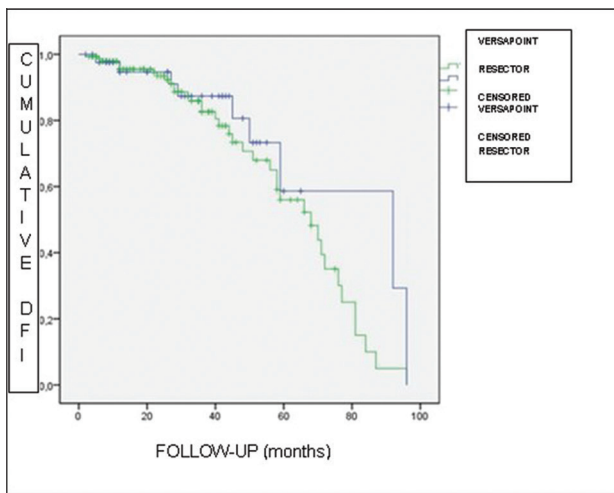
When the type of polyp was studied, 56 (29.01%) were cystic, 54 (28%) glandular, 40 (20.72%) fibroglandular, 20 (10.36%) hyperplastic, 19 (9.84%) fibrous, and 3 (1.55%) focal hyperplasia with a low-grade atypia, and only one (0.52%) case of intermucous focal superficial adenocarcinoma was found. We did not identify significant statistical difference between the histological type and recurrence ( $P = 0.37$ ). The most frequent location of polyps was lateral with 57 (29.54%) cases, 46 (23.83%) on the anterior uterine face, 35 (18.13%) in the fundic, 45 (23.32%) on the posterior face, and 10 (5.18%) in the cornual. Regarding the number of polyps in the Versapoint® group, 117 unique polyps were resected; for 23 women, we resected two polyps; and for 11 women, more than two polyps were resected. In the resectoscopy group, 30 unique polyps were resected; there

**Table 1: Follow-up duration of the patients after hysteroscopic polypectomy**

Follow-up duration (years)	n (%)	P
<1	50 (26)	0.000
1-2	27 (14.4)	0.000
2-3	50 (25.9)	0.000
>3	64 (33.2)	0.000

were two women with two polyps and six women with more than two polyps. A significant statistical difference between the number of polyps and recurrence was not found with Chi-square test ( $P = 0.36$ ). The data about the risk factors for recurrence after hysteroscopic polypectomy are summarized in Table 1.

The average appearance of the first recurrence in the Versapoint® group was  $21.95 \pm 17.79$  months (95% CI= 16.41–27.59) (42 cases) and in the resectoscopy group was  $32.45 \pm 28.15$  months (95% CI= 13.54–51.37) (11 cases). The rate of first recurrence for the Versapoint® group was 25.16% and for the resectoscopy group was 21.42%. The existence of significant statistical differences between recurrence and polypectomy type could not be studied given that the samples were not homogeneous for the hysteroscopist expertise, the type of polypectomy with regard to the varying polyp size, menopausal status, and use of tamoxifen. The recurrence rate for the polypectomy type and the comparison among them are reflected in Table 2. The recurrence and the disease-free interval were both studied using a Kaplan–Meier test [Figure 1], in which we observed that the appearance of the first recurrence was delayed in resectoscopic polypectomy in comparison with the Versapoint® group, without a significant statistical difference in the Mantel–Cox test (mean:  $72.97 \pm 7.33$  months vs.  $61.48 \pm 3$  months;  $P = 0.21$ ).



**Figure 1:** Representation of the disease-free interval after hysteroscopic polypectomy

Significant statistical differences were found between the follow-up duration variable and total recurrence (OR = 2.58; 99% CI = 1.68–50.04;  $P = 0.000$ , Chi-square test) and between the follow-up duration and the appearance of new polyps ( $P = 0.03$ , Chi-square test). The overall rate of new polyps was 26.94%.

## DISCUSSION

It is difficult to retrospectively determine whether the recurrence after hysteroscopy developed near or far from the previous polyp. In our study, the criteria were the appearance of the same histopathological type of polyp on the same uterine face. The recurrence rate appears to be related to the surgical technique, with 15% exclusively mechanical and 0%–4.5% using electrosurgery.<sup>[5]</sup> In our study, the overall rate of the first recurrence was 24.35%; 80.9% corresponded to Versapoint® and 19.1% corresponded to resectoscopy. No significant differences were found. Studies have found that resectoscopy can be associated with recurrences of 0% compared with mechanical instrumental removal at 15%.<sup>[5]</sup> There is no research that would indicate a correlation between any of the currently available electrosurgical devices and polyps' recurrence. In our study, the first rate of recurrence for resectoscopy was high (21.42%). The first rate of recurrence after Versapoint® was also high (25.16%). To reduce the risk of electrosurgery and recurrence, an intrauterine morcellator was suggested. It is very safe and efficient and has lower recurrence rates, despite the larger size and a larger number of polyps on average to treat compared with electrosurgery.<sup>[1,6,7]</sup> The study by Lara-Domínguez *et al.*<sup>[8]</sup> found a higher percentage of relapses with Versapoint® compared with diode laser at 3 months (32.6% vs. 2.2%;  $P = 0.001$ ). Laser treatment was concluded to be efficient in the prevention of recurrences.

The recurrence rate after the hysteroscopic polypectomy was related to the duration of the follow-up duration,<sup>[2,3]</sup> Paradisi *et al.*<sup>[2]</sup> obtained a recurrence rate at 2 years of 13.3%, and Henriquez *et al.*<sup>[9]</sup> found 18.3% recurrence during the 1<sup>st</sup> year; however, Nathani and Clark<sup>[10]</sup> showed that the rates ranged from 2.5% to 3.7% at 9 years.

Yang *et al.*<sup>[3]</sup> investigated the symptomatic factors that influenced recurrence after hysteroscopy. The study revealed

**Table 2: Recurrence of polyps according to the type of polypectomy**

Polyps recurrence	Recurrence rate (%)	Versapoint® (%)	Resectoscope (%)	Versapoint® versus resectoscope P (Wilcoxon test)
1 <sup>st</sup>	24.35	38 (80.9)	9 (19.1)	0.620
2 <sup>nd</sup>	4.1	5 (62.5)	3 (37.5)	0.258
3 <sup>rd</sup>	2.6	3 (60)	2 (40)	0.307
4 <sup>th</sup>	1.05	2 (100)	0	0.470

The first column represents the number of recurrences during the follow-up duration



**Table 3: Risk factors for recurrence after hysteroscopic polypectomy**

Risk factors for recurrence	OR	CI	P
Follow-up duration >3 years	2.58	1.68-50.04	0.000
Abnormal uterine bleeding	2.25	1.1-30.0	0.04
Polyp's size >15 mm	1.63	1.3-3.1	0.02

OR: Odds ratio, CI: Confidence interval

that the number of polyps and the duration of the follow-up duration were significantly associated with recurrence. In addition, a strong positive association was found between polyp recurrence and endometriosis. In a study by Zheng *et al.*, at 2 years, the recurrence rate was 23.08%, and at 5 years, the rate was 56.41%.<sup>[11]</sup>

In our study, we obtained a high first recurrence rate (24.35%) independent of the polypectomy type, which could be explained by the retrospective nature of the study and by the fact that it only included women undergoing hysteroscopy. The women who experienced a symptomatic recurrence were more likely to present for consultation and therefore to more frequently undergo hysteroscopy, for which our population could be at a high risk of recurrence.

With respect to the symptomatic risk factors predicting recurrences, the study by Yang *et al.*<sup>[3]</sup> found that age, parity, BMI, high blood pressure, diabetes, tamoxifen, hormone therapy, and menopausal status did not appear to be related to recurrence. The risk of recurrence appeared to be independent of the presence of AUB or the number and diameter of the polyps, in the study by Paradisi *et al.*<sup>[2]</sup> In our study, the possible risk factors found were symptomatology (specifically AUB), a follow-up duration of longer than 3 years, and a polyp >15 mm [Table 3]. The recurrence of endometrial polyps reached a total of 29.7% for tamoxifen users in the study of Gao *et al.*<sup>[12]</sup> Age, polycystic ovarian syndrome, obesity, and the use of estrogen without opposition from progestogen are considered independent risk factors. In our study, we found no significant association; we found that a higher number of polyps were associated with obesity. Treatment using thyroid hormone in the postmenopausal hypothyroidism has been suggested as a risk factor;<sup>[13]</sup> however, we did not find a significant association with recurrence in our study.

In relation to the histological type, Paradisi *et al.*<sup>[2]</sup> showed that recurrence risk is significantly greater in hyperplastic polyps without atypia compared with benign polyps (43.6% vs. 8.3%). In our study, we did not identify a significant association between histological type and recurrence.

Our study presents certain limitations such as a retrospective study and a higher tendency toward consultation undergoing a hysteroscopy in case of symptomatic women which

prevented us from the diagnosis of asymptomatic women with recurrent polyps. Other limitations that could contribute to the high recurrence rate could be the heterogeneity of the follow-up duration, the different sized sample for the polypectomy type, and the impossibility to compare recurrence by type of hysteroscopic polypectomy, due to the existence of confounding factors. The main concern has to do with the degree of confidence one can have while making a determination between recurrent and *de novo* polyp. We considered that a data point derived based on the description collected from an operative note was sufficiently accurate and/or specific to allow for a sound determination that the newly formed polyp was a recurrent polyp or a *de novo* polyp. We think the best way would be to use video recordings of the initial polypectomy and compare it to hysteroscopy when a new polyp is encountered, but we did not have that possibility for office hysteroscopy.

## CONCLUSION

The rate of first recurrence after a hysteroscopic polypectomy was 24.35%. There was a strong positive correlation between the recurrence and the follow up duration. There were no differences in polyps' recurrence among the types of hysteroscopic polypectomy. The main risk factors for recurrence were polyps causing abnormal uterine bleeding, size, and follow up duration.

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## Conflicts of interest

There are no conflicts of interest.

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