ORIGINAL ARTICLE: GYNECOLOGY AND MENOPAUSE

High number of endometrial polyps is a strong predictor of recurrence: findings of a prospective cohort study in reproductive-age women

Fang Gu, M.D.,[a] Huanxiao Zhang, M.D.,[b] Simin Ruan, M.D.,[c] Jiamin Li, M.D.,[d] Xinyan Liu, M.D.,[a] Yanwen Xu, M.D.,[a,e] and Canquan Zhou, M.D.[a,e]

[a] Center for Reproductive Medicine, Department of Obstetrics and Gynecology, [b] Division of Gynecology, Department of Obstetrics and Gynecology, and [c] Department of Medical Ultrasonics, Institute of Diagnostic and Interventional Ultrasound, First Affiliated Hospital of Sun Yat-sen University; [d] Department of Obstetrics and Gynecology, Second Affiliated Hospital of Guangzhou Medical College; and [e] Key Laboratory of Reproductive Medicine of Guangdong Province, Guangzhou, People's Republic of China

Objective: To compare the incidence of recurrence between a cohort with a high number (≥ 6) of endometrial polyps (EPs) and a single-EP cohort among reproductive-age patients after polypectomy.
Design: Prospective observational cohort study.
Setting: Single university center.
Patient(s): Premenopausal women who underwent hysteroscopic endometrial polypectomy were recruited.
Intervention(s): Patients underwent a transvaginal ultrasound scan every 3 months after polypectomy to detect EP recurrence. Kaplan-Meier and Cox regression models were used to compare the risk of recurrence between the two cohorts and analyze the potential risk factors for EP recurrence.
Main Outcome Measure(s): EP recurrence rate.
Result(s): The study enrolled 101 cases with a high number of EP and 81 cases with a single EP. All baseline parameters were similar except that the high number of EP cohort had a slightly lower mean age than the single EP cohort (33.5 [range 30.0–39.0] vs. 36.0 [30.5–43.0] years). The risk of recurrence in the high number of EP cohort was 4.08 (95% confidence interval [CI] 1.89–8.81) times higher than that in the single-EP cohort 1 year after polypectomy, with a recurrence rate of 45.5% versus 13.4%, respectively. A high number of EPs, endometriosis, and previous polypectomy history were independently associated with polyp recurrence.
Conclusion(s): The high number of EP cohort was much more prone to recurrence than the single-EP cohort. A high number of EPs, endometriosis, and previous polypectomy history were independent risk factors for recurrence. A high number of EPs is suggested to be a distinct subgroup with different pathogenesis, which warrants frequent monitoring and prevention. (Fertil Steril® 2017;■:■–■. ©2017 by American Society for Reproductive Medicine.)
Key Words: Hysteroscopy, polypectomy, endometrial polyps, recurrence

Discuss: You can discuss this article with its authors and other readers at https://www.fertstertdialog.com/users/16110-fertility-and-sterility/posts/24342-24618.

Endometrial polyp (EP), a common gynecologic condition for which abnormal uterine bleeding (AUB) is the most common presenting symptom, is defined as localized overgrowth of the endometrial glands and stroma around a vascular core that projects from the surface of the endometrium (1). Its prevalence ranges from 7.8% to 34.9% in routine clinical practice and is higher in infertile women (2).

Intrauterine structural abnormalities are thought to perturb implantation and cause infertility as well as early pregnancy loss (3, 4), and the presence of EPs is suggested to be the most common pathologic finding detected by office hysteroscopy in subjects with recurrent implantation failure (5). The molecular mechanisms of polyps

Received July 4, 2017; revised November 3, 2017; accepted November 22, 2017.
F.G. and H.Z. should be considered similar in author order.
F.G. has nothing to disclose. H.Z. has nothing to disclose. S.R. has nothing to disclose. J.L. has nothing to disclose. X.L. has nothing to disclose. Y.X. has nothing to disclose. C.Z. has nothing to disclose.
Supported by the Key Laboratory of Reproductive Medicine of Guangdong Province (2012A061400003), the Pilot Construction of Reproductive Clinical Research and Transformation Center of Guangzhou (155700011/201508020006), and the National Natural Science Foundation of China (81370765).
Reprint requests: Canquan Zhou, M.D., Department of Obstetrics and Gynecology, Reproductive Medical Center, First Affiliated Hospital of Sun Yat-sen University, No. 58 Zhongshan Road 2, Yuexiu District, Guangzhou 510080, People's Republic of China (E-mail: zhoucanquan@hotmail.com).

Fertility and Sterility® Vol. ■, No. ■, ■ 2018 0015-0282/$36.00

https://doi.org/10.1016/j.fertnstert.2017.11.029

causing infertility are mainly related to defective endometrial receptivity. EPs can induce local inflammatory changes (6, 7), produce glycodelin to inhibit natural killer cell activity, and decrease the expression of essential receptivity molecular markers, such as HOXA10 and HOXA11 (8). Other studies propose that EPs may present an abnormal site that interferes with sperm transportation as well as embryo implantation (9).

In addition to scientific evidence, polypectomy has been proven to increase pregnancy rates of spontaneous conception as well as assisted reproduction in infertile patients (10, 11). As such, clinical practice guidelines recommend mandatory surgical EP removal in women seeking pregnancy because of its negative effect on embryo implantation and the demonstrated benefits of surgical removal (3, 12).

Hysteroscopic polypectomy, now the criterion standard for the diagnosis and treatment of EP, is performed under direct visualization to completely remove EPs but leave the adjacent endometrium intact (13). However, although hysteroscopic resection effectively removes polyps, EP recurrence remains a concern with recurrence rates of 2.5%–43.6% (13–16). As such, it is critical to identify the risk factors for EP recurrence, especially in reproductive-age women desiring future conception, to aid in clinical counseling and decision making.

Limited data are available in the literature that explore risk factors for EP recurrence, in part owing to the time-consuming nature of a prospective cohort study. Only a few retrospective studies to date have explored EP recurrence risk factors, and they have reported conflicting results and mostly focused on postmenopausal women (13, 15, 16). Although some studies have suggested that EP number did not correlate with recurrence potential, those studies included subjects with only 2–3 polyps in multiple-EP cohorts; cases with >5 polyps have never been discussed (13, 17). In contrast, Yang et al. (14) focused a retrospective study for the first time on the EP recurrence potential of reproductive-age women and suggested that a high number of EPs was a strong predictor for recurrence. Yang et al.'s findings suggested that a subgroup with ≥6 polyps could reach a recurrence rate as high as 59% after an average of 18 months of follow-up, which was much higher than those with a single EP or 2–3 EPs with recurrence rates of 35% and 36%, respectively (14). However, the validity of Yang et al.'s study result may have been compromised by the retrospective study design with different follow-up time points. Accordingly, we designed a 1-year prospective cohort study to compare the recurrence rates with a high number of EPs or a single EP and to explore the potential risk factors for EP recurrence among reproductive-age women.

MATERIALS AND METHODS

Study Design and Patient Selection

This single-center prospective cohort study enrolled premenopausal women who had EPs and underwent hysteroscopic polypectomy in the First Affiliated Hospital of Sun Yat-sen University from January 5, 2015, to January 4, 2016. These women were awaiting a future pregnancy, although some did not plan to conceive immediately. The study included two cohorts of subjects, the single-EP cohort and the high number of EP cohort, for comparison of the relative risk of EP recurrence. The study was reviewed and approved by the Institutional Committee of Ethics for Clinical Research and Animal Trials of the First Affiliated Hospital of Sun Yat-sen University, People's Republic of China. There were no conflicts of interest associated with this study.

Inclusion criteria were premenopausal status with a diagnosis of benign EP confirmed by means of hysteroscopy and histopathology with full EP removal. The histology of the EP was confirmed based on the criterion of irregular endometrial glands with thick-walled vessels scattering in fibrous or collagenous stroma (18). The present study intentionally recruited two divergent cohorts of patients with a single versus ≥6 EPs based on the EP number found during the hysteroscopy examination. The rationale for having single versus ≥6 EPs cohorts was based on quartile cutoff point from our pilot study. We observed that the EP number quartile cutoff points among premenopausal EP patients who underwent polypectomy in our hospital were: 1st quartile = 1; 2nd quartile = 2–3; 3rd quartile = 4–5; and 4th quartile ≥6. Therefore, we decided to recruit patients with the lowest quartile of EP numbers (single EP) and the highest quartile of EP numbers (≥6 EPs) as the single-EP cohort versus the high number of EP cohort. Women who received hormone contraception, hormone replacement therapy, controlled ovarian stimulation, and medications that affect the endometrium, such as tamoxifen after surgery, were excluded from the study. Women with atypical or hyperplastic EPs were also excluded.

Office Hysteroscopy

Office hysteroscopy was scheduled in the follicular phase after menstruation (days 5–12 of the cycle) for EP diagnosis and localization. It was performed with the use of a hysterovideoscope (Hopkins II 30°; Storz) with an outer diameter of 5 mm. After speculum application and cervical disinfection, the hysteroscope was introduced intracervically. The uterine cavity was distended with the use of 0.9% sodium chloride solution. The fluid was introduced by means of an automated hysteroscopic distension pump at an inflow pressure of 100–110 mm Hg. The hysteroscopic polypectomy was performed with the use of a small ovum forcep for blunt removal with the help of hysteroscopy for targeting the EPs. The remaining small pedicle was curetted if necessary. Hysteroscopy was used to reinspect the uterine cavity to confirm complete EP removal. The specimen was then sent for histopathology analysis. We avoided using diathermy to prevent deep injury to the endometrium, which might be unfavorable for embryo implantation. All of these procedures were performed exclusively by the same experienced physician (H.Z.).

Patient Enrollment and Data Collection

Subject recruitment occurred when patients returned to obtain their histologic and hysteroscopy reports 2 weeks after office hysteroscopy, and eligible patients were recruited based