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# Evaluation of relationship between endometrial polyp and insulin resistance: A case-control study

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**Abstract**
**Objectives:** Recently insulin resistance (IR) has increasingly attracted attention for its role in promoting endometrial proliferation. This study was conducted to investigate the correlation between endometrial polyps (EP) and IR, and the risk factors.
**Material and Methods:** Retrospective analysis was carried out among patients who underwent hysteroscopy in gynecology and obstetrics department of Macau Kiangwu Hospital during October 2021 and December 2022. According to the pathological results of endometrium, subjects were divided into EP group and control group (normal endometrium). The clinical data and insulin resistance related indicators were compared.
**Results:** 134 patients with EP and 98 control patients were included in this study. When compared with control patients, the percentage of irregular menstruation or amenorrhea was higher, the waist circumference was wider, the serum fasting insulin (FIN) level and insulin resistance index (HOMA-IR) were higher in EP patients, and the difference was statistically significant ($p$<0.05). Logistic multiple regression analysis showed that FIN, HOMA-IR, abdominal obesity and irregular menstrual cycle were risk factors for endometrial polyps.
**Conclusions:** Patients with EP own some characteristics of IR, and IR may be related to the occurrence and development of EP, which should attract enough attention from patients. Lifestyle adjusting, paying attention to menstruation, and adding insulin sensitizer when necessary are recommended.

**Keywords:** Endometrial polyp, insulin resistance

## Introduction
Endometrial polyp (EP) is a local hyperplasia of endometrial stroma and glands. It forms sessile or pedunculated protrusions on the surface of the endometrium [1]. As a common benign disease among women of childbearing age, it is reported to be an important factor leading to abnormal uterine bleeding and infertility. However, most patients have no obvious symptoms in clinical practice, and it is only found in occasional pelvic ultrasound examination [2]. At present, the pathogenesis of EP is not clear, which may be related to genetic factors, estrogen and progesterone receptor imbalance, cell proliferation/apoptosis imbalance, immune inflammatory stimulation and other factors [3, 4]. Existing studies have found that patients with metabolic abnormalities such as diabetes and hyperlipidemia are the high risk population of endometrial proliferative diseases such as EP, endometrial hyperplasia and endometrial cancer [5, 6]. As the core pathophysiological change of such metabolic diseases, insulin resistance (IR) has increasingly attracted attention for its role in promoting endometrial proliferation. The purpose of this study was to investigate the incidence of IR in patients with EP and its related influencing factors.

## Materials and Methods
### Research object
Retrospective analysis was made on the patients who were hospitalized in Obstetrics and Gynecology Department of Macau Kiangwu Hospital from October 2021 to December 2022 for undergoing hysteroscopy due to abnormal uterine bleeding or/and abnormal echo or intrauterine occupying lesions displayed by ultrasound. The medical history in detail and the relevant clinical data were recorded.

**Inclusion criteria**

1. There are indications for hysteroscopy and no contraindications.
2. Normal endometrium or endometrial polyp confirmed by hysteroscopy and endometrial pathology.

**Exclusion criteria**

1. Patients with diabetes or abnormal glucose tolerance, hyperlipidemia, polycystic ovary syndrome.
2. Have taken hormone drugs in recent 3 months.
3. There are contraindications to hysteroscopy.
4. Recurrence of endometrial polyps.
5. Pathology indicates endometrial hyperplasia, endometrial carcinoma, submucous myoma of uterus, endometritis. All patients signed the informed consent form, and the study was approved by the hospital ethics committee (Approval No. 2022-05).

**Serum test**

All subjects fasted for more than 8 hours and collected elbow vein blood in the morning of admission: ① the serum insulin (FIN) was detected by German ACS180 SE chemiluminescence immunoassay analyzer and matching reagents; ② Fasting plasma glucose (FPG) was detected by glucose oxidase method in Tosoh Corp of Japan.

**Calculation index** ① body mass index (BMI) = square of body mass/height (kg/m2); ② HOMA-IR: HOMA-IR=FIN x FPG/22.5; ③ Fasting blood glucose/insulin ratio (G/I): G/I=FPG/FIN.

**Surgical procedures and specimen handling**

On the day of operation, hysteroscopic diagnostic curettage or electrotomy was performed under intravenous general anesthesia. The specimens were sent to the pathology department, fixed with 10% formalin solution, embedded in paraffin, and stained with hematoxylin eosin (HE). Diagnosis of endometrial histopathology was made according to WHO criteria 2014 [7].

**Grouping**

The patients were categorized, according to the pathological results, into the endometrial polyp group (polyp group) and the normal endometrial group (control group) respectively.

**Statistical treatment**

The data of this study were input into Excel chart, and analyzed by SPSS 22.0 statistical software. The measurement data of normal distribution was expressed by (mean ± SD). The mean between groups was compared by independent sample t-test, and the rate between groups was compared by chi-square test. The risk factors of endometrial polyps were screened by multivariate logistic regression analysis. $p<0.05$ means the difference is statistically significant.

**Results**

**Comparison of general conditions of two groups of patients**

This study enrolled 232 patients, including 134 patients with endometrial polyps and 98 patients with normal endometrium. There was no significant difference between the two groups in terms of age, pregnancy/parity, body mass index (BMI), hip circumference, waist hip ratio, hypertension, endometrial staging (proliferation/secretory phase). The proportion of irregular menstruation or amenorrhea in endometrial polyps patients was higher than that in normal patients, and the waist circumference was wider. The difference was statistically significant ($p<0.05$).

**Table 1:** Comparison of general conditions of two groups of patients

| | Polyp group (n=134) | Control group (n=98) | P |
|---|---|---|---|
| Age(years) | 36.10±9.12 | 35.08±7.44 | >0.05 |
| **Gravidity** | | | |
| ≤1 time(n) | 62 | 46 | >0.05 |
| ≥2 times(n) | 72 | 52 | |
| **Parity** | | | |
| ≤1 time(n) | 94 | 70 | >0.05 |
| ≥2 times(n) | 40 | 28 | |
| Menstrual cycle | | | |
| Regular(n) | 87 | 76 | <0.05 |
| Irregular/Amenorrhea(n) | 47 | 22 | |
| **Hypertension** | | | |
| Yes(n) | 8 | 8 | >0.05 |
| No(n) | 126 | 90 | |
| BMI(kg/m$^2$) | 23.01±3.14 | 21.63±5.27 | >0.05 |
| Waist circumference/WC (cm) | 78.14±5.48 | 71.44±6.74 | **<0.05** |
| Hip circumference/HC (cm) | 91.01±8.60 | 87.69±6.28 | >0.05 |
| Waist hip ratio(WC/HC) | 0.82±0.15 | 0.81±0.22 | >0.05 |
| **Endometrial staging** | | | |
| Proliferation phase(n) | 82 | 63 | >0.05 |
| Secretory phase(n) | 52 | 35 | |

**Comparison of IR related indexes between two groups**

The serum FIN and HOMA-IR of patients with endometrial polyps were significantly higher than those of the control group ($p<0.05$), while the serum FPG and G/I ratio had no significant

difference. See Table 2 for details.

**Table 2:** Comparison of IR related indexes between two groups

| IR related index | Polyp group | Control group | P |
|---|---|---|---|
| FPG (mmol/L) | 5.28±0.65 | 5.43±0.82 | > 0.05 |
| FIN (mIU/L) | 8.60±0.76 | 7.38±0.40 | < 0.05 |
| HOMA-IR | 2.09±1.56 | 0.91±0.45 | < 0.05 |
| G/I | 0.82±0.34 | 0.89±0.51 | > 0.05 |

**Logistic multiple regression analysis of risk factors for endometrial polyps**

Take the single factor analysis content in the results in 2.1 and 2.2 as the data sample of multifactor analysis. Take endometrial polyps as the dependent variable, and the factors with statistical significance in Table 1 and Table 2 as the independent variable, then assign values (1=endometrial polyps, 0=normal endometrium), and finally establish a logistic multiple regression analysis model. The results show that FIN, HOMA-IR, abdominal obesity (waist circumference ≥ 80 cm) Irregular menstrual cycle/amenorrhea is a risk factor for endometrial polyps ($p$<0.05, see Table 3 for details)

**Table 3:** Logistic multiple regression analysis of risk factors for endometrial polyps

| Influencing factors | β | SE | Wald$\chi^2$ | OR | OR（95% CI） | P |
|---|---|---|---|---|---|---|
| FIN≧10mIU/L | 0.871 | 0.228 | 13.921 | 2.383 | 1.505-3.725 | 0.007 |
| HOMA-IR≧2.14[8] | 0.810 | 0.290 | 7.588 | 2.242 | 1.265-4.002 | 0.005 |
| Waist circumference ≧80cm | 0.608 | 0.174 | 12.401 | 1.831 | 1.301-2.570 | 0.016 |
| Irregular menstrual cycle / amenorrhea | 0.555 | 0.189 | 8.921 | 1.762 | 1.213-2.544 | 0.015 |

## Discussion

Endometrial polyp is a focal benign proliferative lesion of endometrium composed of a small amount of dense fibrous connective tissue, which is common in women of childbearing age and pre/post menopause, and is one of the main reasons for abnormal uterine bleeding [9]. At present, surgical resection is the main treatment in clinical practice, but its etiology and pathogenesis are still unclear. The postoperative recurrence rate is high, and there is a certain probability of malignant transformation [10]. Existing studies suggest that the occurrence of endometrial polyps is related to genetic factors, endocrine disorders, estrogen and progesterone receptor disorders, cell proliferation/apoptosis imbalance, immune inflammatory stimulation and other factors [3, 4]. Metabolic syndrome, as a complex of multiple metabolic disorders (obesity, hypertension, hyperlipidemia, diabetes or abnormal glucose tolerance), has a clear relationship with the occurrence of endometrial cancer, and its core pathophysiological changes (IR) play an important role in pathogenesis [5, 11, 12]. However, there are few studies on the relationship between IR and endometrial cancer precursor diseases (endometrial polyps and endometrial hyperplasia).

Olga, *et al*. [13] studied and included 100 perimenopausal patients with abnormal uterine bleeding. The incidence of HOMA-IR and IR in endometrial polyps group was significantly higher than those without endometrial lesions. Ozkan *et al*. [14] found in the study of postmenopausal endometrial polyps that the levels of FIN and HOMA-IR in endometrial polyps patients were higher than those in the control group. Logistic regression analysis showed that metabolic syndrome was still closely related to EP even excluding the effects of hormone therapy, IR, and serum Insulin levels. Flavia *et al*. [15] suggested that obesity, dyslipidemia, hyperglycemia and metabolic syndrome may be predictive factors for endometrial polyps in postmenopausal women. Recently, Serdar *et al*. [6] found that FBG ≥ 110mg/dL and HOMA-IR > 2.34 can increase the risk of endometrial polyps and/or endometrial hyperplasia by 5 times and 2 times respectively. Feng *et al*. [16] found that FIN, 2-hour Insulin and HOMA-IR in endometrial polyps patients were higher than those in non EP patients, which was positively related to the occurrence of EP. Logistic regression analysis of EP-related factors showed that IR was a high-risk factor for EP. In the follow-up study of the same research team, the endometrial thickness of EP patients with IR after taking metformin for 2 years became thinner than that before treatment, suggesting that improving IR is helpful to reverse endometrial hyperplasia [17]. In this study, patients with endometrial polyps have the following characteristics compared with those with normal endometrium: 1) The proportion of irregular menstruation or amenorrhea is higher; 2) Waist circumference is wider; 3) The blood FIN was higher; 4) HOMA-IR is higher. According to the results of Logistic regression analysis, FIN ≥ 10 mIU/L, HOMA-IR ≥ 2.14, waist circumference ≥ 80cm, irregular menstrual cycle or amenorrhea are risk factors for endometrial polyps. We consider that patients with endometrial polyps have some characteristics of IR, and IR may be related to the occurrence and development of EP.

IR refers to the decrease in the efficiency of insulin in promoting glucose uptake and utilization due to various reasons, and hyperinsulinemia caused by the compensatory secretion of excessive insulin by the body to maintain the stability of blood sugar [18]. Insulin is a major anabolic hormone that promotes cell proliferation and can directly play the role of growth factor through its receptor; Obesity, especially abdominal obesity, fat accumulation in the trunk can increase aromatase activity, reduce sex hormone binding globulin (SHBG) synthesis, increase free estrogen in serum, and work with Insulin on endometrial cells to promote their mitosis and inhibit cell apoptosis [19]. Insulin can also promote insulin like growth factor (IGF-1), which is an important factor to promote cell proliferation. For premenopausal patients, long-term hyperinsulinemia can lead to abnormal ovarian androgen secretion, chronic anovulation, and relatively insufficient progesterone, which can not fully antagonize the proliferation of estrogen on the endometrium, and then endometrial lesions and even canceration [15].

## Conclusions

To sum up, endometrial polyps are closely related to IR, so patients should pay enough attention to it, adjust their lifestyle, pay attention to menstruation, and use insulin sensitizer when

necessary may effectively avoid recurrence and malignant change.

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**Ethical statement**
All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors. Informed consent was obtained from all individual participants included in the study.

**Conflict of Interest Statement**
The authors have no proprietary, financial, professional, or other personal interest of any nature in any product, service, or company.

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