

# **PCOS- Concerns for Tomorrow**

**Endometrial Hyperplasia & Endometrial Polyp**

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# **Questions to be answered**

**Is there a connection between**

**PCOS & Endometrial Polyp and hyperplasia ?**

**And**

**Management of Endometrial polyp and Endometrial  
Hyperplasia**

# Evaluating the Association Between Endometrial Cancer and Polycystic Ovary Syndrome

Zeina Haoula; Maisa Salman; William Atiomo

Hum Reprod. 2012;27(5):1327-1331.

## Abstract and Introduction

### Abstract

**BACKGROUND** Given the current lack of clarity in the published literature, we performed a systematic review of the literature to determine the exact strength of the association between polycystic ovary syndrome (PCOS) and endometrial cancer (EC).

**METHODS** All published studies on the association between PCOS and EC identified through MEDLINE (1966–April 2011), EMBASE (1980–April 2011) and Cochrane (1998–April 2011). Original data were abstracted where available and summarized on a separate Microsoft Excel (2007) database for analysis. A total of 14 studies comparative and non-comparative were identified and included.

**RESULTS** The non-comparative and comparative data suggested that women with PCOS were more likely to develop EC. A meta-analysis of five comparative studies showed an increased risk of EC in women with an odds ratio of 2.89 with a 95% confidence interval of 1.52–5.48.

**CONCLUSIONS** Women with PCOS are about three times more likely to develop EC compared with women without it. This translates into a 9% lifetime risk of EC in Caucasian women with PCOS compared with 3% in women without it. Although most women (91%) with PCOS will not develop endometrial cancer, our study has shown that they are more likely at increased risk. More studies are required to clarify the exact molecular mechanisms, determine the best way of screening and preventing disease progression.

## **Polycystic ovary syndrome and increased polyp numbers as risk factors for malignant transformation of endometrial polyps in premenopausal women.**

Kilicdag EB<sup>1</sup>, Haydardedeoglu B, Cok T, Parlakgumus AH, Simsek E, Bolat FA.

### **Abstract**

#### **OBJECTIVE:**

To determine the pre-malignant and malignant potential of endometrial polyps and to assess whether different clinical parameters are associated with malignancy in the polyps of premenopausal women.

#### **METHODS:**

The clinical records of operative office hysteroscopic and resectoscopic procedures for endometrial polyps in 417 premenopausal women who attended Baskent University were examined over a retrospective period of 30 months. Only premenopausal patients were included in the study.

#### **RESULTS:**

In 97.8% of women, histology showed benign endometrial pathology. In 2.2% of women, pre-malignant or malignant conditions were found in the polyp. Polycystic ovary syndrome (PCOS) and the presence of 2 or more polyps were associated with significant pre-malignant or malignant changes.

#### **CONCLUSION:**

The presence of irregular vaginal bleeding was not a predictor of malignancy in the polyp. Premenopausal women with PCOS and those with 2 or more polyps had an increased prevalence of polyp malignancy. These groups of patients, whether symptomatic or not, should be evaluated by hysteroscopic resection of the polyps.

## **The percentages of endometrial hyperplasia and endometrial cancer among polycystic ovary syndrome (PCOS) patients presenting with abnormal menstrual pattern.**

Prakansamut N, Sirayapiwat P, Triratanachat S.

### **OBJECTIVE:**

Assess the occurrence of endometrial hyperplasia and endometrial cancer among PCOS patients having abnormal menstrual pattern. Endometrial thickness and other clinical characteristics associated with endometrial hyperplasia and endometrial cancer were also evaluated

### **MATERIAL AND METHOD:**

Women with PCOS and abnormal menstrual pattern were enrolled into this cross-sectional study. Endometrial thicknesses were evaluated using transvaginal sonography. Endometrial aspiration was performed with endometrial aspirator and sent for pathology.

### **RESULTS:**

Out of 52 PCOS patients with abnormal menstrual pattern, nine (17.3%) and one (1.9%) had endometrial hyperplasia and endometrial cancer, respectively. There was no significant difference in mean endometrial thickness between those who had abnormal and normal endometrium (8.19 +/- 2.58 mm and 7.76 +/- 4.03 mm, respectively). However BMI and age of patients with abnormal endometrium were significantly higher and older than those with normal endometrium ( $p = 0.031$  and  $p = 0.009$ , respectively).

### **CONCLUSION:**

Nineteen point two percent (19.2%) of patients with PCOS and abnormal menstrual pattern had endometrial hyperplasia or endometrial cancer. Endometrial thickness was not different between those with abnormal and normal endometrium.

## Risk factors for Endometrial Cancer in women with PCOS

- Anovulation leading to unopposed estrogen stimulation of the endometrium
  - Obesity,
  - Insulin resistance
  - Diabetes
  - Nulliparity
- Hardiman P, Pillay O, Atiomo W. Polycystic ovary syndrome and endometrial carcinoma. *Lancet* 2003;361:1810–1812.

# Endometrial polyps

Incidence 7.8% to 34.9%

## Risk factors

Age – is best documented risk factor

Obesity

Tamoxifen use – 30-60% prevalence

Infertility

Risk of malignancy – 0.2 TO 12.9 %

Asymptomatic polyp – 1.51%

Symptomatic polyp – 4.47%

AUB is the commonest symptom

# Endometrial Polyps – Diagnosis

- TVUS in proliferative phase is the most reliable

- Sensitivity 86%
- Specificity 94%
- Positive predictive value 91%
- Negative predictive value 90%

- Vercilleni et al Hum Reprod 1997;12:1768-71

- Colour flow Doppler

- single feeding vessel is typical
- Increases the sensitivity and specificity

- IU contrast by saline infusion sonography

- 3D –USG – limited improvement

- Hysteroscopy and guided biopsy /excision biopsy

# Endometrial Polyps – Management

- Spontaneous regression in 25%
  - Smaller polyp more likely to regress compared to >10 mm long polyp
- Use of LNG IUS in women taking tamoxifen can prevent polyp formation
- Blind Dilatation and curettage
  - Removes polyp only in 4% cases
  - Adding polyp forceps --- removes in 41%

# Endometrial Polyps – Management

- Hysteroscopic resection is the gold standard for the treatment
- Effective and safe
- Should be the method of choice in symptomatic pre and post menopausal women
- Asymptomatic women – can consider observation
- Recurrence after hysteroscopic removal – for upto 9 years follow up
  - 2.5 to 3.7 %

# Endometrial Hyperplasia

- **Main aetiology** – unopposed oestrogen stimulation of endometrium
- **Risk factors**
  - Increased BMI - excessive peripheral conversion of androgens to estrogen in adipose tissue
  - Anovulation as in Peri-pmenopause and PCOS
  - Oestrogen secreting tumour – granulosa cell tumour
  - Drug induced – ERT, Tamoxifen

# Endometrial Hyperplasia - Classification

The revised 2014 World Health Organization (WHO) classification

Two groups based upon the presence of cytological atypia:

**Hyperplasia without atypia**

and

**Atypical hyperplasia**

# Endometrial Hyperplasia - Diagnosis

Histological examination is essential for diagnosis

Endometrial surveillance can be done by endometrial sampling

Outpatient endometrial biopsy is convenient and has high overall accuracy for diagnosing endometrial cancer

Systematic Review --A pooled likelihood ratio (LR) of **12.0 for a positive test** and **0.2 for a negative test result.**

Despite a negative biopsy result, 2% of women will still have endometrial hyperplasia.

# Endometrial Hyperplasia - Diagnosis

- **Transvaginal Ultrasound Scan (TVS)**
- Systematic reviews have suggested
  - At cut-off of 3 mm or 4 mm --the probability of cancer is reduced to less than 1%
  - A larger cut-off value has been suggested for women taking HRT or tamoxifen

Timmermans A, et al. *Obstet Gynecol* 2010;116:160–7

# Endometrial Hyperplasia - Diagnosis

- The role of **ultrasound in premenopausal women**
  - Is restricted to identifying structural abnormalities
  - There is overlap between normal endometrial thickness and that caused by endometrial disease.
  - For women with PCOS and absent withdrawal bleeds or abnormal uterine bleeding, RCOG guidelines concluded that **7mm cut off**, below this cut-off endometrial hyperplasia is unlikely

# Endometrial Hyperplasia - Diagnosis

## Role of Hysteroscopy

Systematic review of data from 26 346 women.

A positive hysteroscopy result increased the probability of cancer to 71.8% from a pretest probability of 3.9%,

A negative hysteroscopy result reduced the probability of cancer to 0.6%.

Hysteroscopy is more accurate in detecting than excluding endometrial disease and has a higher accuracy for endometrial cancer than endometrial hyperplasia

Clark TJ, et al, JAMA 2002;288:1610–21.

# Endometrial Hyperplasia Without Atypia Management

- Risk of progressing to endometrial cancer is  $< 5\%$  over 20 years
- Majority of cases will regress spontaneously.
- Reversible risk factors such as obesity and the use of HRT should be identified and addressed if possible.
- Treatment with progestogens has a higher disease regression rate compared with observation alone.
- Progestogen treatment is indicated in women who fail to regress following observation alone and in symptomatic women with abnormal uterine bleeding.

# Endometrial Hyperplasia Without Atypia Management

- **The LNG-IUS** - the first-line medical treatment
  - v/s oral progestones
  - higher disease regression rate
  - more favourable bleeding profile
  - fewer adverse effects.
- **Continuous progestogens**
  - medroxyprogesterone 10–20 mg/day or norethisterone 10–15 mg/day
  - for women who decline the LNG-IUS.
- **Cyclical progestogens should not be used because they are less effective**

# Endometrial Hyperplasia Without Atypia Management

Endometrial surveillance

At a minimum of 6-monthly intervals,

Two consecutive 6-monthly negative biopsies should be obtained  
prior to discharge.

# Endometrial Hyperplasia Role of Hysterectomy

- Hysterectomy is indicated in women
  - Progression to atypical hyperplasia occurs during follow-up,
  - **Patients with atypia**
  - There is no histological regression of hyperplasia despite 12 months of treatment,
  - There is relapse of endometrial hyperplasia after completing progestogen treatment,
  - There is persistence of bleeding symptoms,
  - The woman declines to undergo endometrial surveillance or comply with medical treatment.
- Postmenopausal - a bilateral salpingo-oophorectomy with total hysterectomy.
- For premenopausal women
  - , the decision to remove the ovaries should be individualised
  - **bilateral salpingectomy** should be considered

## Endometrial Hyperplasia Role of Hysterectomy

- There is no benefit from intraoperative frozen section analysis of the endometrium or routine lymphadenectomy.
- Endometrial ablation is not recommended because complete and persistent endometrial destruction cannot be ensured and intrauterine adhesion formation may preclude endometrial histological surveillance.



DR DURU SHAH - PRESIDENT PCOS SOCIETY (OF INDIA )

AND

THE ORGANIZERS