

Concerns of Tomorrow in PCOS - Endometrial Cancer

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Case Summary

30 yr lady married since 5 years went to her ObGyn for irregular scanty menses and breast heaviness. She was moderately obese with a BMI of 30 and some hirsutism.

She was to be put on hormonal therapy initially and hence was asked to see me for her breast complaints.

One of her concerns was the risk of cancer in view of the various hormones likely to be advised to her for her PCOS treatment.

Metaanalysis 1

Chittenden et al 2009

- 8/19 studies chosen for meta analysis evaluating risk of EC, Ov Ca, Br Ca in PCOS pts
- EC OR 2.70 with 95% CI 1-7.29
- Ov Ca OR 2.52 with 95% CI 1.08-5.89
- Br Ca OR 0.88
- Concluded - EC 3X, Ov Ca insufficient evidence, Br Ca no risk

Metaanalysis 2

Z Haoula et al 2012

- PCOS OR 2.89 with 95% CI of 1.52-5.48
- Epidemiological studies showed a 3% lifetime risk of E.C in Caucasian women
- With PCOS the lifetime risk 9%

Metaanalysis 3

P Hardiman 2014

- Assessed risk of EC, Ov Ca, Br Ca
- 11 studies included - 919 with PCOS, 72054 without PCOS

		All ages	<54
EC	OR	2.79	4.03
	CI	1.31-5.9	2.42-6.7
	P	<0.0008	<0.00001
Ov Ca	OR	1.41	2.52
	CI	0.93-2.15	1.08-5.89
	P	<0.11	<0.03
Br Ca	OR	0.95	0.78
	CI	0.64-1.39	0.46-1.32
	P	<0.78	<0.35

Danish Cohort Study

Gyn Oncol 2015

- Danish National Patient Register
- ~12000 Pts with PCOS from 1977-2012
- 279 with Cancer
- EC OR 3.9 - majority type I
- Ov Ca OR 1.8 not significant
- Br Ca OR 1.1
- Kidney, Colon, Brain Ca risks increased

Critique of Meta analysis

- 1. Heterogenous studies - case control studies, cohort studies, observational, studies with no control groups
- 2. In 2 of the meta analysis results skewed due to one study with high OR for EC as well as Ov Ca
- 3. Some studies included were before NIH consensus on PCOS definition, some had self reported diagnosis, PCOS Pts enrolled based on physician diagnosis indicating selection biases
- 4. Some studies had Pts with PCOM but not necessarily PCOS

Confounding Factors

- Obesity - risk factor for EC and Br Ca and some association with Ov Ca. Epidemiological studies show >40% EC due to increased BMI. Additional proportion due to lack of physical activity associated with obesity. Obese people have similar hormonal milieu as PCOS pts
- Diabetes - increases risk of EC secondary to hyperinsulinemia, hyperglycemia and inflammation
- Possibility of a common inherited genetic variant between PCOS and EC
- Other factors maybe age at first pregnancy, parity, use of hormones
- Obese v/s Non Obese PCOS
- Anovulatory v/s Ovulatory PCOS

Risk Reducing Strategies 1

Screening

Oligo- or amenorrhoea in women with PCOS may predispose to endometrial hyperplasia and later carcinoma. It is good practice to recommend treatment with gestogens to induce a withdrawal bleed at least every 3 to 4 months.

Transvaginal ultrasound should be considered in the absence of withdrawal bleeds or abnormal uterine bleeding. In PCOS, an endometrial thickness of less than 7 mm is unlikely to be hyperplasia.

A thickened endometrium or an endometrial polyp should prompt consideration of endometrial biopsy and/or hysteroscopy.

There does not appear to be an association with breast or ovarian cancer and no additional surveillance is required.

Risk Reducing Strategies 2

Lifestyle changes - to reduce obesity and to increase physical activity

It is recommended that lifestyle changes, including diet, exercise and weight loss, are initiated as the first line of treatment for women with PCOS for improvement of long-term outcomes and should precede and/or accompany pharmacological treatment.

Physical activity and EC risk

- Meta analysis from Netherlands Cancer Institute in 2007
- Physical activity associated with reduction in risk of EC (>20%) independent of BMI.
- Dose Response effect with physical training associated with HR of 0.1-0.5 i.e. 50-90% risk reduction
- Pooled estimate of 27%
- Mech of action of physical activity - decrease insulin, decrease oestrogen, increase immune cells

Risk Reducing Strategies 3

Metformin use?

Insulin-sensitizing agents have not been licensed in the UK for use in patients without diabetes. Although a body of evidence has accumulated demonstrating the safety of these drugs, there is currently no evidence that the use of insulin-sensitising agents confers any long-term benefit.

Use of weight reduction drugs may be helpful in reducing hyperandrogenaemia.

Points to Ponder

- Generally low incidence of EC in Indian population at present - so even with the increased risk of 3X the overall risk low
- High incidence of breast ca in western population (1 in 8/10). Is it because of this high incidence no increased risk seen with PCOS as there is a definite increased risk with obesity alone
- Require large prospective longitudinal cohort study to prove association between PCOS and Ca