ENDOMETRIOSIS ASSOCIATED MALIGNANCY

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OBJECTIVE

Does such an entity really exist	What are the risk ratios & risk factors	Any specific EAM defining criteria
Most common EAM & subtypes	Any prevention modality	Clinical implications for treating professionals

Disease Burden

- Endometriosis: Wilbur MA *et al.* 2017
  - 5 -15% reproductive age women
  - 3 - 5% postmenopausal women
- Probable malignancies associated with endometriosis (EAM): Krawczyk N *et al.* 2016, ESHRE guidelines
  - Overall: RR 1.07
  - Ovarian – 80%
  - Extra-ovarian: 20%

  (Endometrium, Breast, Cutaneous melanoma, Intestine, Rectovaginal septum, Abdominal wall, Pleura, Brain, Thyroid, Kidney)

Overall risk is very low

Not statistically significant

Origin From Endometriosis

1. Evidence of endometriosis close to tumor
2. Exclusion of invasion from other sources
3. Presence of tissue resembling endometrial stroma surrounding characteristic epithelial glands
4. Presence of transition from benign to malignant changes

- Krawczyk N *et al.* 2016
- Sampson B *et al.* 1925
- Scott *et al.* 1953

Possible Pathophysiology

- Inflammation: Chronic + Acute
  - Infiltration of endometriosis in surrounding tissue > Periodic hemorrhage > Increased local macrophages and cytokines > Cellular proliferation + Immune dysregulation
- Hyper estrogenic state:
  - Increased aromatase in endometriotic implants > Increased E2 > b catenin pathway > Cellular proliferation > Atypical endometriosis (Intermediate precursor lesion) > Progression to malignancy

- Krawczyk N *et al.* 2016
- Chen B *et al.* 2024

Possible Pathophysiology

- Common genetic alterations:
  - LOH, PTEN, ARID1A, p53, PIK3CA, KRAS, Hormonal receptors

	Absolute risk of developing cancer in a woman's lifetime		Increase in risk in women with endometriosis
	All women	Women with endometriosis	
Ovarian cancer	1.3 %	2.5 %	+1.2 %
Breast cancer	12.8 %	13.3 %	+0.5 %
Thyroid cancer	1.3 %	1.8 %	+0.5 %

ESHRE guidelines

Decreased risk of cervical cancer

ESHRE guidelines

ENDOMETRIOSIS ASSOCIATED OVARIAN CANCER (EAOC)

Presently, the diagnostic gold standard for Endometriosis continues to be invasive laparoscopy followed by histological examination

Aim is to improve prevention, early detection, precise diagnosis,

and treatment approaches, thereby optimizing the clinical outcome for patients with EAOC

ENDOMETRIOSIS ASSOCIATED OVARIAN CANCER (EAOC)

- RR: 1.37 compared to general population
- AR: 2.5% compared to general population
- 1% premenopausal women with endometriosis
- 1 – 2.5% postmenopausal women with endometriosis

- Krawczyk N *et al.* 2016
- Chen B *et al.* 2024

ENDOMETRIOSIS ASSOCIATED OVARIAN CANCER (EAOC)

- Factors associated with increased risk
  - Duration of the disease surpasses 10 years after the initial diagnosis
  - Frequent occurrence of ovarian endometriosis
  - Size of endometrioma >/= 9 cm
  - Postmenopausal status
  - Primary infertility

- Krawczyk N *et al.* 2016
- Chen B *et al.* 2024
- Kobayashi *et al.* 2008
- ESHRE guidelines

ENDOMETRIOSIS ASSOCIATED OVARIAN CANCER (EAOC)

- Ovarian cancer types:
  - Endometroid carcinoma: 85 – 90% associated with endometriosis
  - Clear cell carcinoma: 50 - 74% associated with endometriosis
  - Low grade serous
  - High grade serous and Mucinous: No association

- WHO FGT 2020 5th edition
- Wilbur MA *et al.* 2017
- Krawczyk N *et al.* 2016
- Kim HS *et al.* 2014
- Pearce CL *et al.* 2012

Common somatic mutation

Not predictive of future development of malignancy

ESHRE guidelines

Overall risk is very low

Routine screening only

CLINICAL IMPLICATIONS

1. EAOC is characterised by early age onset

2. Commonly a low-stage and low-grade disease

usually without ascites at initial presentation .

3. Significantly better prognosis (DFS and OS)

CLINICAL IMPLICATIONS

A possibility of malignant transformation should be included in diagnostic

considerations for patients with endometriosis , especially

in postmenopausal women who present a sudden recurrence

of symptoms.

CLINICAL IMPLICATIONS

Because of the malignant potential, endometriosis

patients should, if indicated, receive a combined estrogenprogestin

therapy (HRT, hormone replacement therapy) or tibolone

even after hysterectomy; unopposed estrogens should generally

be avoided in these patients .

CLINICAL IMPLICATIONS

Clinicians should be aware of the increased risk of specific subtypes of ovarian carcinoma in endometriosis patients

All patients with atypical endometriosis should be referred to gynae-oncologist

Treatment related risk ……..

Long-term hormonal treatment

Associated with increased and decreased risk of some cancers

Not increased risk of endometriosis associated malignancy

Complete surgical excision

may decrease risk of endometriosis associated ovarian cancer

Risk benefit should be considered

ESHRE guidelines

Management of endometriosis associated ovarian cancer is not different from those not associated with endometriosis

- **Krawczyk N *et al.* 2016**
- **Chen B *et al.* 2024**

Take home message

- Increased risk: Ovarian, Breast and Thyroid only
- Low Absolute increase risk – Routine population based screening
- Decreased risk of cervical cancer
- Associated ovarian cancer – mainly Endometroid, Clear cell and Low grade serous
- Mucinous and High grade serous are never associated with endometriosis

Take home message

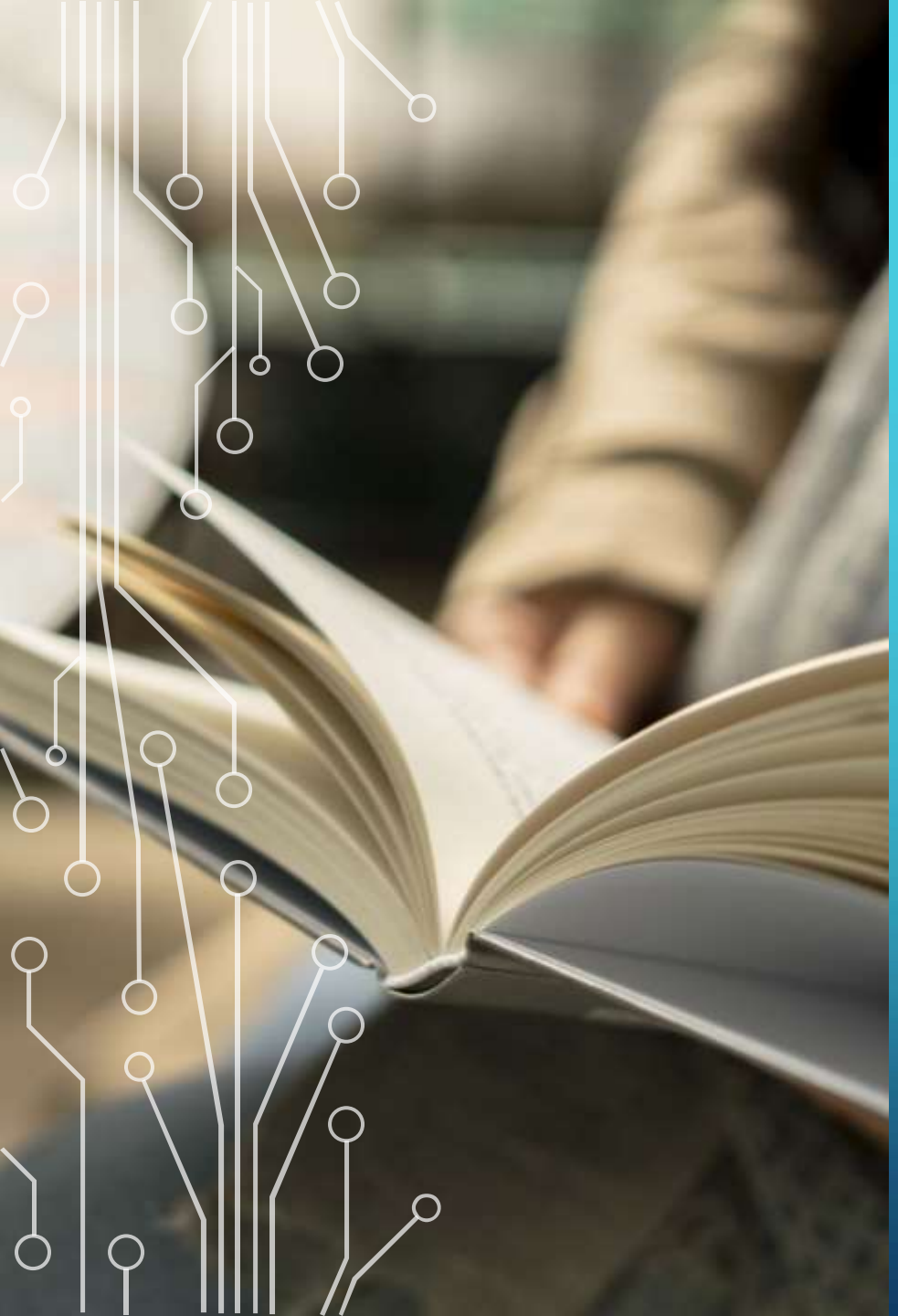
- Ovarian cancers associated with endometriosis – Favourable clinic-pathological features and favorable prognosis

- Proposed pathophysiology for the development of cancer in endometriotic implants
- Genetic analysis of endometriotic tissue – Can not predict future development of malignancy

Take home message

- No definite tool to predict future development of malignnacy
- Long-term hormonal treatment – No association with increased cancer risk
- Complete surgical excision – May decrease cancer risk
- Management of endometriosis associated ovarian cancers is same as that of non endometriosis associated
- Individualized approach

THANK YOU



SUGGESTED READING

1. *New insights about endometriosis-associated ovarian cancer:* *pathogenesis, risk factors, prediction and diagnosis and treatment :Biqing Chen, Liping Zhao, Rulin Yang and Tianmin Xu* Department of Obstetrics and Gynecology, The Second Hospital of Jilin University, Changchun, China*

2. *Endometriosis-associated Malignancy*

   N. Krawczyk1, M. Banys-Paluchowski1,4, D. Schmidt2, U. Ulrich3, T. Fehm1

3. *ESHRE 2022 GUIDELINES*