EDITORIAL

DOI: 10.52054/FVVO.2024.13577
Facts Views Vis Obgyn 2025;17(1):3-4

Is it time to re-evaluate how we speak to women with endometriosis about their risk of ovarian cancer

Thomas Edward Ind

Head of Department of Gynaecological Oncology, Royal Marsden Hospital, London, United Kingdom

Keywords: Endometriosis, endometriomas, ovarian cancer

The lifetime risk of all ovarian cancers in women is about 1.3% (1 in 77) with that reported in women with endometriosis to be 1.8% (1 in 56).[1] A more recent meta-analysis confirmed the association with the strongest relationship occurring with type 1 histological sub-types.[2] There is an 160% increased risk of cardiovascular disease if a woman is menopausal accompanied by the risks of surgery, most authors feel that the increased risk of ovarian cancer secondary to endometriosis does not warrant surgical intervention. Recent ESHRE guidelines state that "….clinicians reassure women with endometriosis with regards to their cancer risk….".[3]

However, the same guideline states that "….there is epidemiological data, mostly on ovarian endometriosis, showing that complete excision of visible endometriosis may reduce the risk of ovarian cancer….".[3]

The association between endometriosis and ovarian cancer is greater than the proportion of cases that fulfil the Sampson criteria[4] for Endometriosis Associated Ovarian Cancer (EAOC) and is thought to be related to combinations of inflammation, oxidative stress, oestrogens, and genomic alteration via the KRAS, P13K pathways with alteration in ARID1A and PTEN. For this reason we more commonly associate EAOC with clear cell, endometrioid, and low-grade serous types of cancers (type 1) with odds ratios previously being reported as high as 3.73, 2.32, and 2.02 respectively.[5]

A more recent study has looked at the 'typology' of endometriosis and the ovarian cancer risk by assessing 78,476 women with endometriosis on the Utah Population Database matched against those women without endometriosis on a 1 to 5 ratio.[6] In this later study, the median follow-up in women with endometriosis was 8 years and 14 years for women without endometriosis. The adjusted hazard ratio for any endometriosis and the development of epithelial ovarian cancer was 4.20 [confidence interval (CI): 3.59-4.91)].

However, women with deep infiltrative endometriosis and endometriomas had the highest hazard ratios for epithelial ovarian cancer of 9.66 (CI: 7.77-12.00). This increased risk involved all epithelial ovarian cancers including high grade serous carcinomas which have previously not been associated with endometriosis. The adjusted hazard ratio for type 1 ovarian cancers was 18.96 (CI: 13.78-26.08).

Corresponding Author: Thomas Edward Ind, MD, Head of Department of Gynaecological Oncology, Royal Marsden Hospital, London, United Kingdom
E-mail: ThomasInd@mac.com **ORCID ID:** orcid.org/0000-0001-5260-199X
Received: 31.07.2024 **Accepted:** 15.12.2024 **Publication Date:** 28.03.2025

Cite this article as: Ind TE. Is it time to re-evaluate how we speak to women with endometriosis about their risk of ovarian cancer. Facts Views Vis Obgyn. 2025;17(1):3-4

As with other registry based studies, the Utah Study's strength lies in the large number of patients.[6] However, the diagnosis of endometriosis itself is not a rigorous one with some patients diagnosed on symptoms alone, others by laparoscopic interpretation and others by histology. Histologically proven endometriosis can be in a

number of different sites and can be superficial or deep or it can be in the form of endometriomas. Registry based clinical studies are not without their own instrinsic failings.

They often lack in data quality and are variable in detail. Furthermore there are often failings in active follow-up.[7] In this subject, known confounding factors such as contraceptive pill usage and tubal ligation are not accounted for.

The significance of any new data lies in how practice could change as a result. With type 1 ovarian cancers accounting for about 20% of all cases and therefore occurring in about 1 in 400 women, even with a hazard ratio of nearly 20, any intervention could result in at best 20 people receiving treatment to prevent one case. Either way, this could be presented in plain language to a patient wishing to make an informed decision and balanced along with symptoms, fertility wishes and risks of surgery. There is some evidence that excision of endometriosis (especially endometriomas) may be protective against the risk of EAOC.[8,9] However, the extent of protection is controversial and does not take into account other environmental factors and hormone usage that may also influence malignant transformation.

This study will no doubt prompt analyses of other large patient cohorts. If these figures are confirmed, then we will have to re-think how we counsel women with a history of deep infiltrative endometriosis and endometriomas. This is especially in those women who are nearing the end of their menstrual life and who have completed their family. Furthermore, an understanding of the molecular differences between women with endometriosis that eventually do lead to EAOC and those that do not might help us understand which patients to offer prophylactic surgery to.

Acknowledgements: None.

Footnotes

Financial Disclosure: The author declared that this study received no financial support.

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