



Endometriose nun doch Präkanzerose?



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Vorkommen

EAM – Endometriose assoziierte Malignität

- Ca. 1% aller Endometriose – Patientinnen

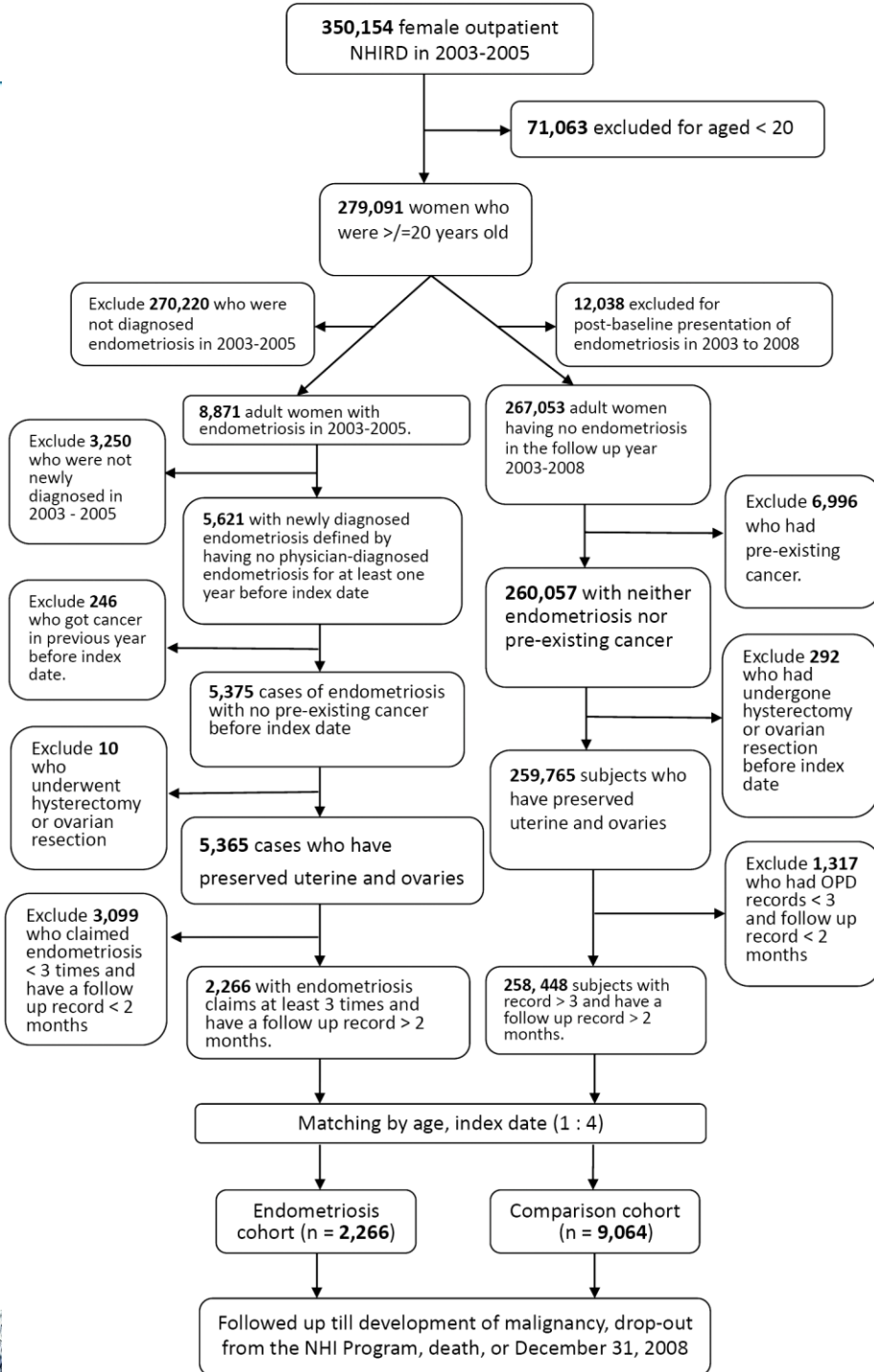
Hum Reprod 1992;7

- 20% extragenital
(Darm, rektovaginales Septum, Vagina,
Bauchdecke, Peritoneum, Omentum, Pleura,
Brust, Non-Hodgkin Lymphome, u.a.)

Heidemann et al, Acta Obstet Gynecol Scand. 2014;93

EAM - Vorkommen

Lokalisation	Intestinum	Haut	Harntrakt	Peritoneum
	Rektum/Sigma 37%		Blase 8%	
	Appendix 17%		Ureter 3%	
	Ileum 6%			
	Bruchsack 2%			
Gesamt	62 %	22 %	11 %	5 %



The Risks for Ovarian, Endometrial, Breast, Colorectal, and Other Cancers in Women With Newly Diagnosed Endometriosis or Adenomyosis

A Population-Based Study

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TABLE 3. Measured HRs stratified by endometriosis sites for selected types of cancer using multivariate Cox proportional hazards regression model

Study cohort	Cancer (x/y)				
	Ovary (13/9), HR (95% CI)	Endometrial (12/5), HR (95% CI)	Breast (18/51), HR (95% CI)	Colorectal (4/6), HR (95% CI)	Others (42/92), HR (95% CI)
Comparison cohort	Reference	Reference	Reference	Reference	Reference
Endometriosis cohort	4.56 (1.72–12.11)	4.05 (1.20–13.66)	1.15 (0.61–2.15)	2.99 (0.72–12.51)	1.12 (0.71–1.75)
Ovarian endometriosis group	4.37 (1.07–17.83)	3.23 (0.54–19.27)	0.54 (0.12–2.40)	—	0.71 (0.32–1.58)
Ovarian + adenomyosis	6.10 (0.71–52.68)	—	—	—	1.39 (0.47–4.09)
Ovarian mixed with other	—	6.37 (0.66–61.87)	2.20 (0.50–9.77)	—	0.75 (0.13–2.43)
Pure ovarian	5.59 (0.67–46.48)	—	—	—	0.44 (0.06–3.22)
Adenomyosis group	5.50 (1.95–15.50)	4.38 (1.22–15.72)	1.24 (0.62–2.48)	3.51 (0.75–16.47)	1.24 (0.76–2.03)
Adenomyosis + ovarian	6.10 (0.71–52.68)	—	—	—	1.39 (0.47–4.09)
Adenomyosis mix other	10.35 (3.07–34.91)	3.91 (0.66–23.21)	1.41 (0.47–4.20)	13.04 (2.21–77.04)	1.55 (0.77–3.11)
Pure adenomyosis	3.25 (0.90–11.82)	5.13 (1.36–19.40)	1.34 (0.62–2.89)	1.55 (0.17–14.25)	1.06 (0.58–1.94)
All other sites group	3.20 (0.64–15.94)	3.37 (0.60–19.07)	0.86 (0.26–2.88)	2.85 (0.31–26.26)	1.16 (0.58–2.34)

Risikofaktoren

- Hyperöstrogenismus - endogen oder exogen
(cave! E2 - Monoth. nach HE bei Endometriosepat.)

Gynecol Oncol. 2000;79:

- protektiv: OC, Geburten, Salpingektomie od HE

Hum Reprod. 2013;28:

Pathogenese

- unklar!
- mehrere Faktoren
 1. Hormone
 2. Cytokine
 3. genetische Komponente

Pathogenese

Table 2 Genetic alterations associated with endometriosis and endometriosis-related malignancies.

Factor	Genetic alteration	Current data
Oxidative stress	8-OHdG	8-Oxo-2'-deoxyguanosine is a marker of oxidative DNA damage. Endometriosis-related ovarian cancer show significantly stronger staining of 8-OHdG than ovarian cancers not accompanied by endometriosis 43 . Endometriotic cysts and atypical endometriosis also stain positive for this marker. 8-OHdG seems to play a role in pathogenesis of ovarian cancer and was linked to poor prognosis 44 .
Tumor suppressor genes	PTEN	Phosphatase and tensin homolog is mutated in many cancer entities, particularly in endometrial and endometrioid ovarian cancer; its inactivation occurs early during tumorigenesis 53 . PTEN somatic mutations are frequently found in endometriotic cysts 45 .
	p53	As a negative cell-cycle regulator, p53 is involved in tumorigenesis of different malignancies. Several studies showed no expression in benign endometriosis but high expression in benign endometriotic lesions next to the endometrioid or clear cell carcinoma 54 .
	ARID1A	ARID1A mutations are significantly more common in two ovarian cancer subtypes associated with endometriosis (clear-cell and endometrioid). In case of endometriosis synchronous with ovarian cancer, mutation was more frequent in clones derived from endometriosis samples directly adjacent of the tumor than in those from distant endometriotic lesions 46 .
DNA repair	hMLH1	hMLH1 corrects errors in DNA replication; hypermethylation of its promoter occurs early in endometrial malignant transformation and can be identified in 10% of typical and in 33% of atypical endometrial hyperplasias 47 . Abnormal methylation can be observed in endometriosis as well 53 .
Oncogene	Bcl-2	Expression of this anti-apoptotic protein is significantly higher in endometriosis accompanying cancer (42–73%) than in benign endometriosis (23%) 54 , suggesting its role in the early steps of tumorigenesis.
	KRAS	KRAS mutations are significantly more common in endometriosis-associated endometrioid adenocarcinomas (29%) than in tumors not associated with endometriosis (3%) 48 .
Chromosomal aberrations	Aneuploidy	Aneuploidic frequency seems higher in endometriosis specimen from patients with advanced endometriosis when compared to the background frequency observed in normal specimens, particularly with regard to chromosome 17, on which tumor suppressor gene p53 is located 49,50 .
Loss of heterozygosity (LOH)		A trend of increasing LOH frequencies has been described between solitary endometriosis lesions, endometriosis-associated carcinoma and endometrioid ovarian cancer, respectively 51,52 . Common LOH events can be identified in endometriosis synchronous with ovarian cancer 45,56 .

JAMA | **Original Investigation**

Endometriosis Typology and Ovarian Cancer Risk

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Endometriose und Ovarialkarzinomrisiko

Table 2. Risk of Ovarian Cancer Histotypes Among Women With vs Without Endometriosis (N = 450 906)

Ovarian cancer diagnosis	No. of ovarian cancer cases in women		Multivariable-adjusted, RD (95% CI) ^{a,b}	HR (95% CI)	
	With endometriosis (n = 78 476)	Without endometriosis (n = 372 430)		Unadjusted	Multivariable-adjusted ^a
All epithelial ovarian cancers	225	372	9.90 (7.22 to 12.57)	3.64 (3.10 to 4.26)	4.20 (3.59 to 4.91)
High-grade serous ^c	71	222	1.35 (0.08 to 2.63)	2.02 (1.56 to 2.62)	2.70 (2.09 to 3.49)
Low-grade serous ^c	<11	<11	0.28 (-0.17 to 0.73)	7.33 (2.18 to 24.63)	8.12 (2.67 to 24.73)
Endometrioid	67	48	3.89 (2.45 to 5.33)	7.87 (5.52 to 11.22)	7.96 (5.59 to 11.34)
Mucinous	21	28	1.42 (0.42 to 2.43)	4.42 (2.56 to 7.62)	4.56 (2.64 to 7.90)
Clear cell	30	15	1.39 (0.56 to 2.21)	10.90 (6.02 to 19.74)	11.15 (6.19 to 20.10)
Carcinosarcoma	<11	<11	0.44 (-0.03 to 0.91)	5.69 (2.25 to 14.38)	6.24 (2.62 to 14.89)
Other epithelial ^d	23	47	0.89 (0.06 to 1.73)	2.96 (1.84 to 4.79)	3.34 (2.05 to 5.44)

Abbreviations: HR, hazard ratio; RD, risk difference.

^a Multivariable-adjusted models are adjusted for birth state, birth year, age at first endometriosis diagnosis, and parity. None of these variables had missing values.

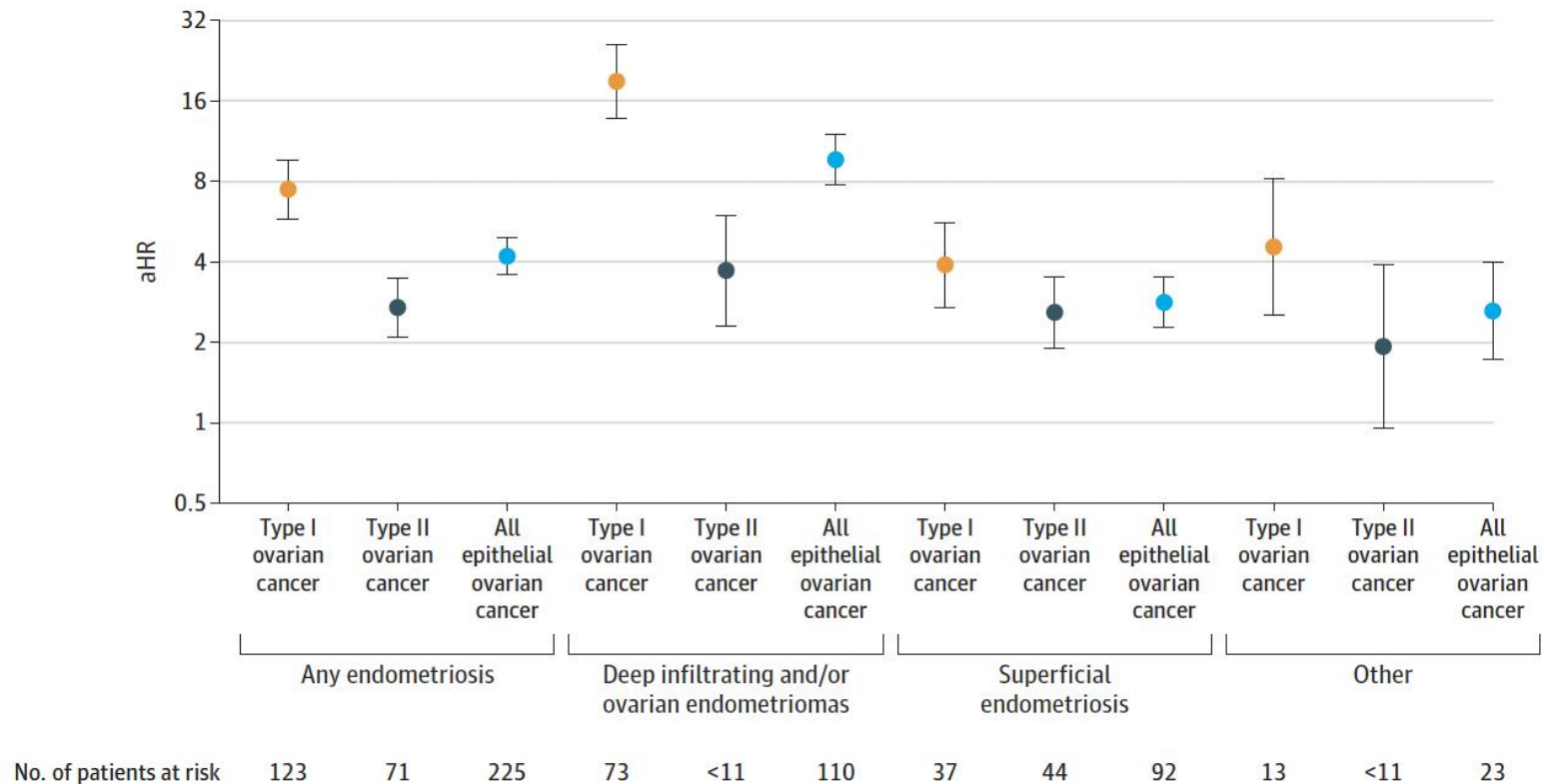
^b RD is reported as the number of cases per 10 000 people.

^c Per Utah Department of Health and Human Services confidentiality requirements, counts less than 11 are not reported and any counts that could be used to calculate those less than 11 for another category are not provided.

^d Other epithelial ovarian cancer includes those with histology codes 8010, 8032, 8046, 8140, 8230, 8290, 8440, 8560, 9111, 8255, 8323, and 9000.

Endometriose und Ovarialkarzinomrisiko

Figure 2. Adjusted Hazard Ratios (aHRs) Comparing Risk of Ovarian Cancer Among Women With vs Without Endometriosis



Results for each endometriosis subtype are presented separately for all histotypes of ovarian cancer: type I (endometrioid, clear cell, mucinous, and low-grade serous) and type II (high-grade serous). Although a positive association was observed for all possible combinations of endometriosis subtypes and ovarian cancer histotypes, the association between deep

infiltrating and/or ovarian endometriomas and type I ovarian cancer was greatest in magnitude. Per Utah Department of Health and Human Services confidentiality requirements, counts less than 11 are not reported and any counts that could be used to calculate those less than 11 for another category are not provided. Whiskers indicate 95% CIs.

Endometriose und Ovarialkarzinomrisiko

- Relevanz für die Praxis?

Absolute Risikodifferenz:

10 – 27 zusätzliche Fälle pro 10 000 Frauen = 0,2%

Lebenszeitrisiko ca. 1%

ChatGPT 5.2 ▾



2024 10 JAMA - Endometriosis Typ...
PDF

kritisiere diese Arbeit wissenschaftlich

Stärken

- Sehr große Kohorte
- Differenzierte Subtyp-Analyse
- Methodisch anspruchsvolle Statistik
- Relevante Fragestellung

Zentrale Schwächen

- Keine Kausalität
- Wahrscheinlicher Surveillance- und Reverse-Causation-Bias
- Fehlende Schlüsselkonfounder
- Überbetonung relativer Risiken
- Klinische Schlussfolgerungen gehen über die Daten hinaus

Kurzfasit

Die Arbeit zeigt robuste **Assoziationen**, überschätzt jedoch vermutlich deren **kausale und klinische Bedeutung**. Sie ist hypothesisengenerierend – nicht praxisverändernd.

A large, rugged mountain peak with a forested valley below. The mountain is covered in light-colored rock and snow, with deep shadows in the crevices. The sky is a clear, deep blue. The foreground shows a dense forest of evergreen trees on a lower slope.

Danke