

Endometriosis: not just a benign disease

Citation for published version (APA):

Hermens, M. (2022). Endometriosis: not just a benign disease: Insights in the association between endometriosis or adenomyosis and cancer. [Doctoral Thesis, Maastricht University]. Ridderprint. https://doi.org/10.26481/dis.20220627mh

Document status and date: Published: 01/01/2022

DOI: 10.26481/dis.20220627mh

Document Version: Publisher's PDF, also known as Version of record

Please check the document version of this publication:

 A submitted manuscript is the version of the article upon submission and before peer-review. There can be important differences between the submitted version and the official published version of record. People interested in the research are advised to contact the author for the final version of the publication, or visit the DOI to the publisher's website.

• The final author version and the galley proof are versions of the publication after peer review.

 The final published version features the final layout of the paper including the volume, issue and page numbers.

Link to publication

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these riahts.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
 You may freely distribute the URL identifying the publication in the public portal.

If the publication is distributed under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license above, please follow below link for the End User Agreement:

www.umlib.nl/taverne-license

Take down policy

If you believe that this document breaches copyright please contact us at:

repository@maastrichtuniversity.nl

providing details and we will investigate your claim.

Impact paragraph

IMPACT PARAGRAPH

This chapter discusses the valorisation potential of the research presented in this thesis. The clinical and research implications were already addressed in the introduction, the discussion of this thesis and throughout the individual chapters. In this paragraph we will summarize relevance and implications of our research.

An estimated 714,000 women were diagnosed with ovarian or endometrial cancer worldwide in 2020.1 Ovarian cancer, often called "the silence lady killer", is mostly diagnosed in advance stage and has the highest mortality rate of all gynaecological cancers.^{1,2} Unfortunately, efforts to developing screening methods for ovarian cancer were unsuccessful.³ Endometrial cancer is the most common gynaecological cancer, and incidence is increasing due to global increase in obesity, life expectancy and hormone replacement therapy.^{1.4.5} Both diseases have a major impact on women's lives and their families, as well as on health care and health care costs. To prevent these diseases, it is first necessary to identify women at increased risk of developing these cancers. Possible risk factors for both ovarian and endometrial cancers are endometriosis and adenomyosis. The aim of this thesis was therefore to elucidate the association between ovarian or endometrial cancer and endometriosis or adenomyosis and to explore prognosis and preventive options. Our studies showed an increased incidence of both ovarian and endometrial cancer in women with histologically proven endometriosis and adenomyosis. In addition, we found a better survival after both ovarian and endometrial cancer diagnosis in women with endometriosis or adenomyosis. Finally, we reviewed possible involved immunological processes and we found that women with endometriosis who had both ovaries with fallopian tubes removed had a lower incidence of extra-ovarian cancers.

Scientific impact

Our studies, which to our knowledge have examined the largest endometriosis/ adenomyosis cohort to date, strengthen and complement the scientific work on endometriosis or adenomyosis linked with ovarian or endometrial cancer. However, many women have endometriosis or adenomyosis, but the majority will never develop ovarian or endometrial cancer. This thesis therefore shows that it is extremely important to conduct further research in order to establish a better risk profile in women with endometriosis or adenomyosis. Thereby creating more clarity and less anxiety in women with endometriosis or adenomyosis.

In addition, our review of immunological processes involved in the development of endometriosis-associated ovarian cancer showed that there is a knowledge gap on this particular topic. Therefore, our research group initiated a study on possible immunological factors involved in the development of endometriosis-associated ovarian cancer. This may further contribute to our understanding of this association and may help to develop a more appropriate risk profile. Furthermore, our study of ovarian cancer incidence after both ovarian and fallopian tube removal (which can be somewhat synchronized with endometriosis removal) was the first study to show that surgical removal of endometriosis could have a preventive effect on ovarian cancer risk. If future research can ensure that we can select the women with the highest ovarian cancer risk, surgery might therefore be offered to these women as a preventive option.

Our research has been presented at various international and national conferences, as well as local meetings of both gynaecological oncologists and gynaecologists specialized in endometriosis and adenomyosis treatment. In addition, the various studies have been presented in international peer-reviewed medical journals and in the Dutch journal of obstetrics and gynaecologist (Nederlands tijdschrift voor obstetrie en gynaecologie). Our findings resulted in discussions with experts in the field and reviewers of scientific journals. We believe that this could have motivated other researchers to further investigate this topic.

Clinical impact

The translation of scientific research to the medical field is extremely important. We have therefore discussed this extensively in this thesis. For patients, getting cancer is very stressful and preventing ovarian or endometrial cancer could save a lot of suffering for women and their families. This research is hopefully a first step to prevent these cancers in a specific group of women. In addition, it is important to inform patients with endometriosis or adenomyosis about these associations, but also to emphasize that the absolute risks are low and the majority of women with endometriosis or adenomyosis or endometrial cancer.

By presenting our studies at various conferences and local discussions, we have been able to make gynaecologists aware of the link between endometriosis and adenomyosis with ovarian and endometrial cancer. In addition, we presented suggestions on what to watch out for in women with endometriosis or adenomyosis with regard to ovarian or endometrial cancer risk and discussed possible (preventive) strategies. This could improve gynaecological care for these patients. In addition to gynaecologists, this research also has an impact on other medical professionals involved in the care of women with endometriosis or adenomyosis and ovarian or endometrial cancer such as pathologists. Hopefully they will also be more aware of these associations through our presentations or reading our articles. Finally, this research could also have an impact on patient associations as they hopefully can provide better information with the help of our research.

Societal impact

It is estimated that cancer treatment accounts for at least five percent of all health costs.⁶ In addition, the costs of cancer treatment are only increasing due to new treatments such as immunotherapy. Preventing cancer is of course also associated with costs, but if a good risk selection can be made, prevention could be cost-effective. This could also have a huge impact on women's quality of life, which would reduce absenteeism for this group of women, which is beneficial from a social point of view. Moreover, more and more insurers have preventive programs for various diseases and for them preventive treatment of women with endometriosis or adenomyosis with a high risk of ovarian or endometrial cancer may also be of interest.

Conclusion

In conclusion, this thesis contributed to the first steps in the prevention of ovarian and endometrial cancer in women with endometriosis and adenomyosis by elucidating the association, mapping the prognosis, investigating possible immunological processes and investigating a preventive option. This has had scientific, clinical and social impact. Nevertheless, additional research is needed for clinical implementation and eventual prevention of cancer in women with endometriosis or adenomyosis.

REFERENCES

- 1. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin 2021;71:209-49.
- 2. Howlader N, Noone AM, Krapcho M, et al. SEER Cancer Statistics Review, 1975-2014. In: National Cancer Institute. Bethesda M, ed., 2017.
- 3. Menon U, Gentry-Maharaj A, Burnell M, et al. Ovarian cancer population screening and mortality after long-term follow-up in the UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS): a randomised controlled trial. Lancet 2021;397:2182-93.
- 4. Bray F, Dos Santos Silva I, Moller H, Weiderpass E. Endometrial cancer incidence trends in Europe: underlying determinants and prospects for prevention. Cancer Epidemiol Biomarkers Prev 2005;14:1132-42.
- 5. McAlpine JN, Temkin SM, Mackay HJ. Endometrial cancer: Not your grandmother's cancer. Cancer 2016;122:2787-98.
- 6. Peppercorn J. Financial Toxicity and Societal Costs of Cancer Care: Distinct Problems Require Distinct Solutions. Oncologist 2017;22:123-25.