Identification of pre-malignancies in the endometrium as possible precursor lesions of serous epithelial ovarian carcinoma.

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To identify pre-malignant lesions within the endometrium as precursor lesions of serous epithelial ovarian carcinoma.

Ethical review	Approved WMO
Status	Pending
Health condition type	Reproductive neoplasms male malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON35921

Source
ToetsingOnline

Brief title
Precursor lesions for serous EOC in the endometrium

Condition

- Reproductive neoplasms male malignant and unspecified

Synonym
ovarian cancer, serous epithelial ovarian carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Endometrium, Pre-malignancy, Serous papillary ovarian carcinoma

Outcome measures

Primary outcome

Can precusor laesions be identified in the endometrium of women with serous

epithelial ovarian carcinoma?

Secondary outcome

Not applicable.

Study description

Background summary

Ovarian cancer is the second most frequent cancer and has the highest death rate among gynaecologic cancers in the western world, with a lifetime risk of 1-2%. Serous epithelial ovarian cancer (EOC) is the most common type of ovarian carcinoma and comprises approximately 50% of malignant ovarian neoplasm*s. It is mostly high-grade and accounts for a highly aggressive and rapidly progressive disease. The high mortality to incidence ratio associated with EOC accounts for more deaths than all other gynaecologic malignancies combined. Unlike many cancers, there is no easily clinical identifiable pre-malignant phase of this malignancy making early identification difficult. Although extensive research has focused on this topic for the last 35 years, the aetiology of this cancer remains uncertain.

The hypothesis on the development of ovarian cancer with the endometrium as origin is emerging. It is thought that a precursor lesion of serous ovarian carcinoma originates in the uterus and spreads into the peritoneal cavity via a mechanism as is accepted for endometriosis. However, the endometrial tissue has never been extensively screened in order to reveal a putative precursor lesion in women with serous EOC.

This new hypothesis on the endometrium as possible origin of serous EOC is based on the following observations.
1) Previously, a precursor lesion called endometrial intraepithelial carcinoma (EIC) was identified in the endometrium of women with serous uterus carcinoma. Importantly, the premalignant cells of EIC have a loosely cohesive nature and

are able to spread to intraperitoneal surfaces easily. EIC is identified with peritoneal metastasis without evidence of concordant endometrial carcinoma. It is thought that this precursor lesion could also be responsible for a proportion of the serous EOC.
2) Another interesting observation is that hysterectomy and/or tubal ligation decreases the ovarian cancer risk by 43-46%, suggesting that the origin of ovarian cancer could very well be located within the uterus.
3) The pathologist cannot morphologically differentiate between serous carcinomas from different origins (uterus, fallopian tube, ovaries and peritoneum). Histologically, immuno-histologically and genetically there are many similarities among these tumours. This suggests the possibility of similar pathways of carcinogenesis for these tumours.

To investigate this hypothesis of the endometrium as possible origin for serous EOC, the endometrial tissue should be extensively screened in women with serous EOC. As serous ovarian carcinoma is rapidly progressive, disease is most often already extensively spread at diagnosis and neoadjuvant chemotherapy is needed in the majority of these women before complete debulking surgery is attempted. However, the influence of neoadjuvant chemotherapy on the presence of a putative precursor lesion in the endometrium is not yet known. It is a possibility that these putative precursor lesions disappear because of the chemotherapy and will be overlooked when diagnosis is only based on the endometrial tissue retrieved from debulking surgery after chemotherapy. Therefore, a curettage is suggested in these women in order to retrieve endometrial tissue before the start of the chemotherapy. Since diagnosis of ovarian carcinoma is verified with a diagnostic laparoscopy or explorative laparotomy before treatment is started, this procedure will be preceded with a curettage.

Concluding, conformation of this new hypothesis in a prospective setting would change the current view on the aetiology of ovarian cancer, which could have dramatic implications for diagnosing, treatment and prognosis of patients with this type of cancer. As holds true for other cancer types, early identification and treatment of (pre-) malignant lesions of ovarian cancer could positively influence the prognosis of these women.

Study objective

To identify pre-malignant lesions within the endometrium as precursor lesions of serous epithelial ovarian carcinoma.

Study design

A diagnostic laparoscopy or explorative laparotomy is planned for each patient suspected for serous epithelial ovarian carcinoma. Preceding this diagnostic laparoscopy or explorative laparotomy, a curettage will be performed to

retrieve endometrial tissue from these women before chemotherapy will be started. Namely, this diagnostic operation is mostly followed by neoadjuvant chemotherapy before complete debulking surgery is attempted.

Study burden and risks

The additional burden for the patient is minimal, since the additional duration of the anaesthesia is only 10 minutes. There is a small chance of uterus perforation (0.12-0.14%, Aydeniz et al., 2002). Therefore, in this study the curettage will precede the planned diagnostic laparoscopy or explorative laparotomy to enable screening of the uterus after the performed curettage. In this study the additional risk will be minimal since only experienced gynaecologists will perform this intevention. Afterwards, the patient could have some complaints of pelvic pain or some vaginal bleeding for a maximum of three days.

Contacts

Public
Universitair Medisch Centrum Sint Radboud

Geert Grooteplein zuid 10
postbus 9101, 6500 HB Nijmegen
NL
Scientific
Universitair Medisch Centrum Sint Radboud

Geert Grooteplein zuid 10
postbus 9101, 6500 HB Nijmegen
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

All female patients suspected for serous epithelial ovariancarcinoma in which a diagnostic laparoscopy or explorative laparotomy is planned.

Exclusion criteria

Pregnancy
Hysterectomy in personal hysteroy
Confirmed histological diagnosis other than serous epithelial ovarian carcinoma

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-07-2011
Enrollment:	40
Type:	Anticipated

Ethics review

Approved WMO

Date:	26-07-2011
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL36392.091.11