An observational controlled study on vaginal blood flow and sexual functioning after early stage cervical cancer treatment

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This study will investigate a comparison group of women treated with a conventional (non-nerve sparing) RHL for cervical cancer (CC) at the Academic Medical Centre (AMC). Together with the data collected of women treated with a nerve sparing radical...

Ethical review	Approved WMO
Status	Pending
Health condition type	Reproductive and genitourinary neoplasms gender unspecified NEC
Study type	Observational invasive

Summary

ID

NL-OMON42343

Source
ToetsingOnline

Brief title
Sexuo-physiological functioning after cervical cancer treatment

Condition

- Reproductive and genitourinary neoplasms gender unspecified NEC
- Uterine, pelvic and broad ligament disorders
- Obstetric and gynaecological therapeutic procedures

Synonym
cancer of the cervix, cervical cancer

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: KWF Kankerbestrijding & Stichting Alpe d□Huzes

Intervention

Keyword: cervical carcinoma, sexual functioning, vaginal plethysmography

Outcome measures

Primary outcome

Primary outcome measure: Vaginal pulse amplitude (VPA) in response to sexual stimuli.

VPA will be measured by a vaginal photoplethysmograph. The photoplethysmograph is a menstrual tampon-sized device, containing an orange-red light source and a photocell. The light source illuminates the capillary bed of the vaginal wall and the phototransistor responds to the light backscattered by the vaginal wall and the blood circulating within it. When the signal is connected to an alternating current (AC) amplifier, vaginal pulse amplitude (VPA) is measured, which reflects the phasic changes in vaginal engorgement accompanying each heartbeat, with larger amplitudes reflecting higher levels of vaginal vasocongestion. VPA is a sensitive, specific, and reliable measure of vaginal vasocongestion and is used in earlier studies that observed diminished vaginal blood flow in women with neurological damage and in women after radical hysterectomy (see publication of Pieterse et al, 2008, protocol P05.095). VPA will be recorded continuously during the experimental session.
The stimulus material will be identical to the previous studies. All women will

be exposed to two erotic 5.5 min film excerpts (consisting of videos depicting cunnilingus and intercourse). The erotic films will be preceded by 5 min neutral film (during which a non-erotic documentary film excerpt will be shown). The erotic film excerpts are taken from so-called women-made, female-centred erotic videotapes.

VPA is sampled at 20 Hz across baseline and subsequent trails. A two-pass algorithm for automatic artefact removal (© Molenkamp Technical Support Group University of Amsterdam) is used to analyse the VPA data. After artefact deletion peak-to-trough amplitude is calculated for each remaining pulse. For each 5-minute baseline recording, a mean baseline score per subject is calculated. Mean and maximum VPA for each subject within the entire session is identified (i.e. either within erotic stimulus one or two).

Secondary outcome

Secondary outcome measure: Subjective sexual arousal in response to sexual stimuli.

Subjective sexual arousal will be assessed through 3 self-report ratings that will be collected after each neutral film and after each erotic stimulus. Participants will be asked to indicate on a seven-point Likert scale their feelings of sexual arousal. Extremes of the Likert scale will be 1 *not at all*, to 7 *very strong*.

Furthermore, sexual complaints will be assessed using the Leiden Questionnaire (LQ), Gynaecological symptom module questionnaire of the European Organisation for Research and Treatment of Cancer (EORTC) EORTC QLQ-CX24, and the Female Sexual Function Index (FSFI). General health related quality of life is

assessed by the Quality of Life core questionnaire of the EORTC (EORTC QLQ-C30). The Female Sexual Distress Scale (FSDS) will measure sexually related personal distress. The womens* satisfaction with their sexual relationship was evaluated using the Golombok Rust Inventory of Sexual Satisfaction (GRISS). The presence of anxiety and depressive states will be assessed using the Hospital Anxiety and Depression Scale (HADS). Data obtained will be registered and analyzed using SPSS.

Study description

Background summary

Women that have been treated for cervical cancer reported more sexual complaints, such as diminished lubrication, dyspareunia, vaginal shortening and/or tightening, both in comparison to prior to treatment as well as compared to healthy controls. The primary treatment for women with early-stage (FIGO IA2 * IIA) cervical cancer is radical hysterectomy with pelvic lymphadenectomy (RHL). Nowadays the most used procedure for stage IB and IIA carcinoma of the uterine cervix is a modification of the Wertheim operation with influences of Meigs and/or Okabayashi (RHL-WM or RHL-WO, Piver type III). At the LUMC, since 2001, conducting a nerve sparing RHL (RHL-WM-NS) is the standard way of treatment for early stage cervical cancer. At the Amsterdam Medical Centre, surgery among cervical cancer patients is conducted by means of a conventional radical hysterectomy using the Okabayashi method (RHL-WO).
With the conventional RHL (RHL-WM or RHL-WO), the pelvic autonomic nerves (especially the hypogastric plexus) are damaged. This leads to disrupted autonomic innervation of the bladder, rectum, and the blood vessels in the vaginal wall. Consequently, patients often experience various postoperative symptoms concerning, amongst others, sexual functioning. For example, the (increase in) vaginal blood flow in response to sexual stimuli is innervated by the hypogastric nerve. Damage to the hypogastric nerves disrupts the vaginal response to sexual stimuli, which may result in vaginal dryness during sexual intercourse and dyspareunia. Some of these complaints may be prevented by conducting a nerve sparing RHL, in order to prevent damage to the pelvic autonomic nerves.
A preliminary pilot-study by Pieterse et al. (2008, CME protocolno. P05.095) showed that there was a trend (p=.097) for less disrupted vaginal blood flow in response to sexual stimuli in patients after nerve-sparing RHL (RHL-WM-NS)

compared to women that received conventional RHL because the nerve sparing was conducted without success (RHL-WM). Vaginal blood flow in nerve-sparing RHL showed to be comparable to women after simple hysterectomy (AUE) and women without hysterectomy.
In approximately one third of these women, surgery is followed by postoperative external beam radiation therapy (RT). Postoperative RT is conducted when certain risk factors are observed during surgery and prognosis increases after postoperative RT. It is expected that RT causes vaginal changes due to radiation-induced vaginal fibrosis, stenosis and mucosal atrophy, and may therefore also be related to a decreased vaginal response to sexual stimuli. Previous studies have shown that women that were treated with RT more often reported decreased lubrication, dyspareunia and vaginal shortening and/or tightening (Pieterse 2013; Brand 2006; Jensen 2003). These sexual complaints may be partly explained by a decreased vaginal blood flow response after RT.
Although the results in terms of survival after treatment for low stage cervical carcinoma (surgery, if indicated followed by adjuvant radiation therapy) are reasonably good, morbidity due to treatment, among which long-term sexual problems, is still a matter of concern. Problems with sexuality may affect quality of life. After treatment, several symptoms related to sexual dysfunction appeared to be the primary sources of symptom-induced distress.
This study among women treated with a conventional RHL-WO will make it possible to judge the individual influence of the different treatment modalities on the vaginal response and subjective sexual arousal to sexual stimuli. The results of this study are important in order to develop tailored patient information and support regarding sexuality for women that will be treated for early stage cervical cancer and cervical cancer survivors.

Study objective

This study will investigate a comparison group of women treated with a conventional (non-nerve sparing) RHL for cervical cancer (CC) at the Academic Medical Centre (AMC). Together with the data collected of women treated with a nerve sparing radical hysterectomy for CC without RT (P05.095) and with RT (P10.066), and age-matched healthy controls (P05.095), this study will provide information on the individual contribution of (nerve sparing) radical hysterectomy with or without postoperative radiotherapy as a cause for a disrupted vaginal perfusion response to sexual stimuli after treatment.
The results of this study are important in order to develop tailored patient information and support regarding sexuality for women that will be treated for early stage cervical cancer and cervical cancer survivors.
The assumption is that the group of women treated with a conventional RHL will show a more disrupted vaginal perfusion response on sexual stimuli than the group of women treated with a nerve sparing RHL, while the subjective sexual arousal to the sexual stimuli will be comparable. The group of women treated with nerve sparing RHL will be comparable to the group of healthy controls with respect to the vaginal perfusion response. Furthermore, it will be exploratively investigated whether RT will annihilate the expected preserved

vaginal perfusion response after nerve sparing RHL (due to the possible radiation-induced consequences for the vaginal tissue).

Study design

An observational study will be conducted among women treated with a conventional (non-nerve sparing) radical hysterectomy for CC. Among this group of women, the vaginal pulse amplitude (VPA) and subjective sexual arousal in response to sexual stimuli will be measured using vaginal photoplethysmography. The results obtained in the current study will be compared with the data of a group of women treated with a nerve-sparing RHL without external beam radiation (P05.095) or nerve-sparing RHL without external beam radiation (P10.066) and age-matched historical controls (from P05.095) by using a between (4 subject groups) X within (VPA) study design.
The study will be conducted multicenter: The photoplethysmography will be performed at the LUMC. Also, the study will be coordinated at the LUMC. Participants will be recruited at the AMC.

Study burden and risks

Potential participants will be recruited by reviewing medical files by the principal investigator together with the investigator on main inclusion criteria. Eligible potential participants will receive a letter at their home address concerning information of this study. Women can let the researcher know by e-mail or telephone within two weeks whether they are interested in participation. After two weeks the researcher will contact the women who did not respond, by telephone. Women that are interested to participate will receive explanation about the study in detail on the phone from the researcher and subsequently screened on in- and exclusion criteria. After verbal consent of participation during the telephone call, an appointment will be made and the participant receive questionnaires at home. The participants are asked to fill them in prior to their visit at the LUMC and hand them over after filling in the written informed consent.
Part 1 (duration 0.5 hour): During the first part of the visit, written informed consent will be obtained, in which confidentiality, anonymity and the opportunity to withdraw from the experiment without penalty is assured, prior to measurements. The participants* written consent to participate in the study must be obtained after a full explanation has been given of this protocol. This explanation is delivered together with the informed consent form. After that, the participant hands over the questionnaires. In case menopausal status should be verified, a blood sample is then taken by the medical doctor and principal investigator of this project, an assistant under his supervision or the so-called *blood lab* of the LUMC. Subsequently, the participant will shortly be asked if anything has changed with regard to their health since they were screened by telephone. Furthermore, the researcher will explain all procedures of the vaginal plethysmography in detail. The researcher also shows and

explains the devices used in the genital measurement.
Part 2 (duration 1 hour): Experimental session with neutral and erotic films, and vaginal plethysmography. After this experimental procedure, a brief exit-interview will take place.
Participating in this study will not cause any (physical) harm for the participants. The vaginal plethysmographs are sterilized according to LUMC regulations. It is possible that women find it bothersome to watch the erotic excerpts or inserting the plethysmograph. However, no harmful events due to its use have been documented. The chance that women experience pain while inserting the plethysmograph is most likely very small, because it is small, has the size of a small tampon and is made out of smooth material. Furthermore, subjects may use lubricant to insert the plethysmograph. Subjects can leave the study at any time for any reason if they wish to do so without any consequences. Apart from the expected benefits from for future support of cervical cancer patients, there will be no benefits for the study participants.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

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

Inclusion criteria

Pre-menopausal women who have undergone conventional radical hysterectomy with pelvic lymphadenectomy using the Okabayashi method (RHL-WO) at the AMC for the treatment of early stage cervical cancer (FIGO IA2 * IIA). Women are selected on pre-menopausal status because menopausal status can influence the vaginal bloodflow. Women with a history of cervical cancer can be included if treatment has been completed at least 12 months before. All eligible patients have been treated for FIGO stage IA2-IIA cervical cancer with therapyRHL-WO; have no signs of recurrent or metastatic cervical cancer after 1 year; have not received external beam radiation therapy, intravaginal brachytherapy and/or concomitant chemotherapy; did not have their ovaries removed during surgery; are capable of understanding, reading and writing the Dutch language; are not pregnant; have performance status of WHO 1-2, Karnofsky >60; and are <75 52 years of age. Use of medication and hormonal substitutes is registered.

Exclusion criteria

Women that receive radiotherapy and/or concomitant chemotherapy; had their ovaries removed during surgery; or are pregnant; are not included.

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):	22-10-2015
Enrollment:	30
Type:	Anticipated

Ethics review

Approved WMO Date:	13-01-2016
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 25666
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL54662.058.15
OMON	NL-OMON25666