Sexual rehabilitation after treatment for gynaecological cancer

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General introduction

CHAPTER 1

Gynaecological cancers: epidemiology and treatment

Gynaecological cancers originate in the female reproductive organs. They comprise cancers of the ovary, the uterus, the uterine cervix, and vaginal and vulvar cancers. Histological (sub)types, epidemiological factors, characteristics and risk factors vary greatly between the specific cancer types. In the Netherlands, each year about 4500 women are diagnosed with gynaecological cancers. Among these cases, 1900 are endometrial cancers, followed by 1300 ovarian cancers, 700 cervical cancers, 300 vulvar cancers, and 50 vaginal cancers.[1] Incidence rates for endometrial cancer are rising with ageing of the population and increased rates of obesity, while those of ovarian, cervix and vulvar cancers have been more or less stable. Cervical cancer in particular concerns a predominantly young population with a peak age between 30 and 40 years.[1,2] With screening and prevention, especially HPV vaccination, the incidence of cervix cancer is expected to decrease in future decades.[3,4]

Mainstay of treatment of most gynaecological cancer is surgery, while about 35% of patients with gynaecological cancers are treated with radiation therapy, either as primary or post-surgical treatment.[5,6] Patients with early stage cervical cancers are primarily treated with radical hysterectomy in combination with pelvic lymphadenectomy (RHL), and sparing of the ovaries. Fertility sparing approaches for very young women include uterine conserving measures such as trachelectomy. In case of lymph node metastases, close or involved surgical margins, or high-risk factors found after cervix cancer surgery, postoperative external-beam radiation therapy (EBRT) is indicated, often combined with concurrent chemotherapy and (in case of close vaginal margins) with a vaginal brachytherapy (BT) boost.[7,8] Postoperative EBRT is also indicated in patients with endometrial and vulvar cancers in case of risk factors and/or lymph node metastases, with or without chemotherapy and vaginal BT boost, depending on pathological findings. For patients with early stage endometrial cancer with high-intermediate risk factors, vaginal BT alone is used, with the advantages of minimal morbidity and high local control.

Patients with more advanced stages of cervical cancer, and with the more infrequent cases of vaginal cancer, are treated with primary pelvic EBRT, concurrent cisplatin chemotherapy, and intrauterine and vaginal BT.[5,6] The purpose of BT is to deliver a high dose to the centre of the residual tumour, while sparing surrounding tissues. Image-guided approached to BT have increased pelvic control and survival rates, while reducing the risk of major toxicity.[9,10] For BT, MRI-compatible applicators

are placed in the uterus and vagina, and after MRI scanning an individual treatment plan is made to conform the high-dose region to the tumour volume and keep the dose to normal organs within set limits.

Treatment-induced long-term morbidity and sexual problems

Improved screening methods and effective treatment options have resulted in a substantial number of gynaecological cancer survivors.[11] As a consequence, quality-of-life issues have increasingly gained attention.[12] Gynaecological cancer treatment may induce long-term morbidity such as urinary and defecation problems, fatigue and lymphedema, but also early menopause and the loss of fertility in young women, coping, psychological and social issues related to cancer treatment.[13–16] Furthermore, an important part of the impact of gynaecological cancers and their treatment concerns the women's sexual functioning. Sexual problems have been reported by 23% to 70% of the gynaecological cancer survivors and their partners .[15,17–24] Multiple questionnaires studies showed that the majority of reported problems after treatment concerned a tightened and/or shortened vagina, diminished lubrication, dyspareunia (painful intercourse), post-coital bleeding, reduced intensity of the orgasm, but also decreased sexual activity, interest, desire and satisfaction .[15,18,19,21,22,25–33] A large number of these reported sexual problems can be attributed directly to the vaginal consequences of treatment. Treatment with RHL, for example, sometimes leads to shortening of the vagina and damaged pelvic autonomic nerves may lead to vaginal dryness.[13,18,22,31,34–36] Furthermore, primary EBRT with BT delivers a relatively high dose to the upper vaginal region, which results in atrophy (thinning) of the vaginal mucosa with decreased lubrication and telangiectasia. It also results in adhesions and fibrosis with consequential shortening, and tightening of the upper vagina, and loss of flexibility.[37–44] Furthermore, when sexual problems cause survivors to personally experience significant sexual distress this may lead to the diagnosis of a sexual dysfunction.[45]

In order to investigate and reduce the impact of gynaecological cancer treatment on sexual problems and functioning, the studies described in this thesis have been done to explore what forms of patient support and education and/or specific rehabilitation measures are needed, to improve survivors' sexual recovery. Although surgery has a major impact on sexual functioning, the changes and symptoms caused by intensive EBRT and BT combinations are more profound.[13,15,25,29,31,40–42,46–49] Therefore, the studies have been mainly focused on patients with (advanced) cervical cancer, who are most often treated with primary EBRT and BT, and a predominantly young population.[1]

Sexual distress and related needs after treatment

To date, research into sexual problems of gynaecological cancer survivors has mainly focused on vaginal changes caused by treatment. Only few studies have, however, investigated which factors are associated with the experience of sexual distress that is reported by about one third of the survivors.[18,26,32,50] From a biopsychosocial point-of-view, higher levels of sexual distress can be related, not only to

higher levels of physical problems, such as treatment-induced vaginal symptoms, but also to the higher levels of psychological distress.[51–53] Anxiety and depression after cancer treatment are often reported, as well as and interpersonal problems.[15,24,29,54] Also, even though vaginal symptoms are frequent among cervical cancer survivors, it should be explored why these symptoms do not necessarily induce sexual distress to all survivors.

As a result of treatment consequences and sexual distress, gynaecological cancer survivors may have psychosexual health care needs. From quantitative studies it is known that some survivors hardly received such support from their healthcare providers.[55] Moreover, survey studies showed that many more survivors experience psychosexual healthcare needs compared to the number of women who actually seek help and few studies have focused on the partner's perspective.[21,56,57] Also, sexually distressed survivors' needs may differ from to those who do not experience sexual distress. Therefore, insight is needed in the survivors' and their partners' perspective on sexuality after treatment, current psychosexual support and their unmet needs.

Preserving the vaginal blood flow response

In addition to investigations into sexual distress and supportive care needs among gynaecological cancer survivors, it is important to study whether treatment-induced vaginal changes can be diminished. In recent years, it has been investigated if a nerve-sparing modification of the RHL for cervical tumours could prevent damage to the pelvic autonomic nerves and the sexual problems, possibly associated with this damage.[58,59] In the Netherlands, such a nerve-sparing RHL technique has been developed and used in Leiden since 2000.[59,60] However, empirical evidence that women treated with a nerve-sparing RHL suffer less from a reduced vaginal perfusion response during sexual stimulation compared to women treated with conventional RHL is still lacking. Furthermore, since radiation also leads to impaired function of the vaginal mucosa by causing damage to the microvasculature, it should be examined whether postoperative EBRT obviates any preserved vaginal perfusion response after a nerve-sparing RHL.

Preventing radiation-induced vaginal stenosis

Therapy that minimizes the impact of vaginal radiation damage may also improve the sexual recovery of the cervical cancer survivors. The regular use of a vaginal dilator has been associated with a reduction and prevention of the vaginal shortening and/or tightening, and vaginal adhesions.[39,48,61–66] Notwithstanding the fact that more empirical evidence is needed, dilator use has already become worldwide an essential component of gynaecological cancer survivors' sexual rehabilitation after treatment with radiotherapy.[44,65,67]

The content of patient education on vaginal dilator use, however, varies between articles and guidelines.[65] It is most important to provide a consistent and uniform, evidence-based counselling.[68–70] In two survey studies from the UK and Australia

there was consensus among professionals that women undergoing pelvic RT for gynaecological malignancies should receive information about vaginal dilation.[71,72] There was no consensus regarding the type of health care provider needed to provide support, the most appropriate time interval after RT, the frequency and duration of dilator use, and the content of instructions regarding patients' sexual rehabilitation. Consensus on these aspects is also warranted in order to further investigate the efficacy of a standardized procedure of sexual rehabilitation and dilator use after RT.

Despite the proposed benefits of a regular long-term vaginal dilator use, women have difficulties following the instructions and therefore compliance is poor. Research showed that only 1% to 35% of the gynaecological cancer survivors used a dilator twice a week within the first 12 months following EBRT/BT.[43,64,73–76] According to prior studies, survivors experienced barriers, such as painful insertion or reliving their treatment, and facilitating factors, such as concern about the development of vaginal adhesions.[64,69,75,77] It remains unidentified, however, what determined the compliant survivors to continue and maintain long-term regular dilator use.

Interventions during sexual recovery and vaginal dilator use

Education, instructions, as well as additional support during rehabilitation are needed to help survivors experience less problems during long-term dilator use and while gradually resuming sexual activity, however no published effective methodologies are known.[78,79] A few psychological interventions indicated to be feasible and moderately effective in reducing sexual concerns after gynaecological cancer treatment, but these studies were non-controlled or provided insufficient information to calculate the effect size with.[80–82] There are indications from two small Canadian trials that two psychologist-led group sessions after gynaecological cancer treatment increased dilator use compliance compared to "care as usual" in the short term.[73,74] The interventions, however, did not result in significant differences with regard to sexual functioning and research should aim to enhance efficacy of sexual rehabilitation interventions.

Outline of the thesis

In this thesis experimental, quantitative and qualitative research data is gathered to explore what kind of education and/or support is needed to minimize the impact of gynaecological cancer treatment on sexual functioning, and to improve the survivors' sexual recovery.

In the first part of this thesis, we examine gynaecological cancer survivors' experience with sexual recovery after treatment and unmet needs. In order to gain insight in how to reduce sexual distress it is investigated what biopsychosocial factors are associated with sexual distress by conducting a cross-sectional questionnaire study among cervical cancer survivors in **chapter 2**. Furthermore, since qualitative research can complement and amplify the available quantitative data an interview study among cervical cancer survivors, and partners is described in **chapter 3**. Their unmet needs for psychosexual support are explored.

The second part of this thesis explores the prevention of treatment-induced vaginal changes among gynaecological cancer survivors. In **chapter 4** the vaginal blood flow response during sexual arousal among early-stage cervical cancer survivors after treatment with different types of surgery and/or postoperative radiotherapy is experimentally assessed in a controlled study. To prevent sexual problems due to radiation-induced vaginal changes it is important to provide consistent and uniform, evidence-based counselling with regard to sexual rehabilitation and dilator use. Therefore, in **chapter 5** consensus regarding what patient information and support is needed, is sought using the Delphi-method among expert professionals from all Dutch gynaecological cancer centres. Furthermore, in **chapter 6** an interview study among gynaecological cancer survivors identifies what determines their intention, initiation and maintenance of long-term regular dilator use after treatment with radiotherapy.

In the third part of this thesis, a sexual rehabilitation intervention in combination with a patient information booklet was developed based on the study results described in the previous chapters and by involving all relevant end-users. In **chapter 7** the results of a pilot study to assess the interventions' acceptability and clinical feasibility are reported. Finally, a summary of the results, its limitations and conclusions is discussed in **chapter 8**. Both research and clinical implications for future reference are provided.

Part I

Sexual distress and related needs after gynaecological cancer treatment