Early stage cervical cancer : quality of cancer care and quality of life

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Chapter 6

An observational longitudinal study to evaluate miction, defecation and sexual function after radical hysterectomy with pelvic lymphadenectomy for early stage cervical cancer.

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Based on: Int J Gynecol Cancer 2006; 16:1119-1129

Abstract

Objective: To evaluate the problems with voiding, defecation and sexuality after a radical hysterectomy with or without adjuvant radiotherapy for the treatment of cervical cancer stage I-IIa.

Methods: An observational longitudinal study of self-reported bladder, defecation, sexual problems with a baseline score.

Results: Ninety-four women were included in the study. An age matched control group existed of 224 women. The patients showed significant more negative effects on sexual function compared both with the controls as well as compared with their situation before the treatment throughout 24 months of follow-up. The problems included less lubrication, a narrow and short vagina, numb areas around the labia, dyspareunia, and sexual dissatisfaction. Up to 12 months after the treatment the patients complained significantly more of little or no urge to urinate and diarrhoea as compared with the controls. Adjuvant radiotherapy did not increase the risk of bladder dysfunction, colorectal motility disorders and sexual functions.

Conclusions: We conclude that a radical hysterectomy for the treatment of early stage cervical carcinoma is associated with adverse effects mainly on sexual functioning.

Introduction

State of the art treatment for women with early stage cervical cancer (I-IIa) is a radical hysterectomy with pelvic lymphadenectomy (RHL) with or without adjuvant (chemo) radiation (1). Although RHL has good result in terms of survival, it also has its price: loss of fertility, bladder dysfunction, colorectal motility disorders, lymphedema and sexual dysfunction (2-10).

Autonomic nerve damage during surgery plays a crucial role in the aetiology of this morbidity (11). The effects of the treatment for cervical carcinoma on the women's sexuality and the resulting distress, have recently received some attention (4;12-19). In 1999 Bergmark et al. contacted 256 women with a history of early-stage cervical cancer who had been treated 5 years before and asked them to answer a questionnaire about vaginal changes and sexual function. In this retrospective study they reported vaginal changes, like decreased lubrication and a short vagina, after RHL in 25% of cases (3). Weimar Schultz et al. showed in a comparative and longitudinal study that the sexual response of women treated for cervical carcinoma, was significantly disturbed although current sexual behaviour and motivation for sexual interaction were within the normal range (4). Recently, Jensen et al. published the first longitudinal study, which was partly prospective. It comprised 173 patients with early-stage cervical cancer after RHL, who received questionnaires up to 2 years after the operation. Information about the sexual function before the diagnosis of cancer was obtained retrospectively, one year after the operation. The authors reported that RHL had a persistent and negative impact on patients' sexual interest and vaginal lubrication and that the majority of other sexual and vaginal problems disappeared over a two years period (5).

Furthermore, it is well known that RHL can lead to postoperative urinary dysfunction such as urinary retention, straining or inability to void, and, to a lesser extent, to urge and stress incontinence (6;8). Severe constipation has also been described in 5-10% (6;10).

Finally, it remains controversial whether RHL with or without adjuvant radiotherapy or radiation alone has a more adverse impact on the sexual function of patients (3;20-25). Jensen et al., reported persistent and severe sexual problems throughout the 2 years after radiotherapy with only small changes over time (20). On the other hand the results of Bergmark et al. showed that surgery alone had more adverse effects on sexual function than combined treatment modalities, including surgery and radiotherapy or radiotherapy alone (3). The authors did not comment on this.

To evaluate the symptoms that arise following RHL with or without adjuvant radiotherapy for the treatment of cervical cancer, we performed a prospective study in 2 Dutch university centres. The aim of this study was to determine the prevalence of lymphedema, bladder dysfunction, colorectal motility disorders and sexual dysfunction among women who had been treated for cervical cancer by a RHL.

We compared this group of patients with a group of age-matched controlled women from the general population. Because the effect of adjuvant radiotherapy on late side effects is still unclear, we also compared patients who underwent adjuvant radiotherapy to those who did not.

Patients and Methods

Patients and controls

From May 1998 until January 2003 women with early stage cervical cancer who had to undergo RHL were enrolled in the study. These women were treated in the Leiden University Medical Centre or the University Medical Centre Utrecht. In all cases, a RHL type III was performed through a midline incision. Nerve-sparing surgery was not yet routine practice during the time of the study. Patients with lymph node metastasis, parametrial infiltration, tumour growth in the vaginal surgical margins or a combination of unfavourable tumour size, deep infiltration and lympho-vascular space involvement received adjuvant radiotherapy. Radiotherapy included external pelvic irradiation, brachytherapy or both. Ovaries were not routinely transposed before potential radiotherapy. Data on the treatment results were obtained from the prospective databank. Exclusion criteria were: unable to understand the Dutch language and no follow-up due to living outside the Netherlands. The Medical Ethics Committee of both centres approved the study and all women gave their written informed consent.
The control group consisted of women without cervical cancer and who had not undergone a hysterectomy in the past and were matched for age. They were employees from the hospitals and relatives and friends of these employees. The control group was asked to complete the questionnaire once.

Questionnaire

For this study 14 items of the 21 items self-report Gynaecologic Leiden questionnaire (LQ) were used[31]. The 14 items used in the current study were related to lymphedema (1), sexual function (9), voiding (2) and bowel problems (2). The Gynaecologic LQ was completed before the operation and at 3, 12, and 24 months after the operation. Eight questions (sexual function (7), bowel problems (1)) were answered on a 4 or 5-point Likert-scale ranging from 'never' to 'always'. Four questions (bowel problems (1), voiding problems (2), lymphedema (1)) were answered on a 3-point ordinal scale (yes/sometimes/no). Two questions (sexual function) were answered on a dichotome scale (yes/no). In order to obtain an uniform answering format for all the 14 items, the 3, 4 and 5-point scales were dichotomized. Dichotome answer categories were obtained by adding up the answer categories. Since the score on each item did not indicate that a higher score means more endorsement it depends on the score how the dichotome answer categories were computed: 3-point scale: 'yes and sometimes' versus 'no' or 'no and sometimes' versus 'yes'; 4/5-point scale: 'sometimes, often and always' versus 'seldom and never' or 'often and always' versus 'sometimes, seldom and never'.

[1] At the time of the current study the Gynaecologic LQ was not yet validated. Recently, the validation of the psychometric properties of the items concerning sexual functioning of the Gynaecologic LQ was performed (Chapter 5). The results of that study support the reliability and psychometric validity of the Gynaecologic LQ in the assessment of sexual functioning and vaginal changes in gynaecological cancer patients (Chapter 5).

Data analyses

Sexual function, voiding and bowel dysfunction were analyzed in four ways: before versus after the operation, changes since the operation, premenopausal versus postmenopausal, patient versus control, and radiotherapy versus no radiotherapy.

The responses to the questionnaires were dichotomized and the results are presented as relative risks (RR) and corresponding 95% confidence intervals (CI). RR was calculated as the proportion of women with cervical cancer before the treatment reporting the particular problem divided by the proportion of these women after the surgery. The same was done for the patients versus the controls, radiotherapy versus no radiotherapy and pre menopausal versus postmenopausal. In some cases, the relative risk could not be computed, because of zero counts. When this occurred, we added 1 to each cell of the two by two table (an application of Laplace's rule of succession).

We used the scores from all the sexual function items in the 24 months questionnaire to compare the sexual situation at 24 months after the surgery with the situation before treatment. The possible options were better, no change or worse. The Chi square test was used to test whether the score distributions differed from no change. The analyses were performed using SPSS statistical package 11.0 for windows.

Results

Patients and controls

A total of 94 consecutive women were included in the study. Analysis was performed 2 years after involvement of the last patient. Seventy-three women filled in all the questionnaires, in 21 cases data were not available. Nine women did not return all the questionnaires for unknown reasons, they all had a complete remission and are still alive. Two women moved to another city or country. Ten women died. Of these last women, 9 died as a result of the cervical carcinoma and 1 woman due to a cerebral tumour. The mean age at the time of the operation was 43.3 years (SD 11.0) (Range 21-72 years). The characteristics and distribution of treatment of the patients are shown in Tables 1 and 2. The control group consisted of 224 women. All characteristics of the control group are shown in Table 1. Thirty-one women became postmenopausal because they received radiotherapy or their ovaries were removed. Eleven of them used hormonal replacement therapy (HRT) after the treatment.

Characteristics before operation	Women with Cancer n (%)	Controls n (%)
Total patients	94	224
Total complete questionnaires	73(78)	224(100)
Age		
21-30	9(10)	22(10)
31-40	36(39)	77(35)
41-50	27(29)	67(30)
51-60	11(12)	40(18)
61-70	9(10)	16(7)
71-80	1(1)	0(0)
Marital status		
Married or living with a partner	65(70)	173(77)
Single	13(14)	30(13)
Divorced	12(12)	14(6)
Widow	4 (4)	7(3)

Table 1. Characteristics of patients and controls.

Characteristics	Women with Cancer n* (%)
Hormonal status pre-surgery	
Premenopausal	77(83)
Postmenopausal	16(17)
Hormonal status post-surgery	
Premenopausal	46(50)
Became postmenopausal	31(33)
Postmenopausal	16(17)
FIGO	
Ia	5(6)
Ib	79(87)
IIa	5(6)
IIb	2(2)
Ovaries	
Left in situ	67(72)
Removed	26(28)
Adjuvant radiotherapy	
No	58(62)
Yes	36(38)
External	12(13)
Brachytherapy	1(1)
External & brachytherapy	23(25)
HRT	11(12)

Table 2. Treatment characteristics of the cervical cancer patients. * Total number varies between 91-94, because of missing data.

Patient before surgery versus patient after surgery

The absolute numbers, RR and corresponding 95% CI for all items are shown in Table 3.
Patients had significantly more lymphedema 3 months after the treatment up to 24 months follow-up. At the 3 months follow-up, a significantly larger percentage of the patients complained of little or no urge to urinate. After 12 months follow-up a significantly larger percentage of the patients reported moderate urine incontinence. Only after 24 months follow-up a significantly larger percentage of the patients complained of "little or no lubrication" during sexual arousal compared to the pre-surgery levels. Compared to the situation before the operation, throughout the first 24 months a significantly larger percentage of the patients reported complaints of pain during coitus, a short vagina, numb areas around the labia, dry vagina during coitus and dissatisfaction with sexual relationship.

No/total no.responding (%)

Characteristics	Before surgery Patient	3 Months Patient	RR(95%CI)	12 Months Patient	RR(95%CI)	24 Months Patient	RR(95%CI)
Often diarrhoea	1/94(1)	5/93(5)	5.1(0.6-42)	4/77(5)	4.9(0.6-43)	2/73(3)	2.6(0.2-28)
Often constipation	3/94(3)	3/93(3)	1.0(0.2-4.9)	4/77(5)	1.6(0.4-7.1)	3/73(4)	1.3(0.3-6.2)
Little/no urge	0/93(0)	10/93(11)	**11(1.5-84)***	5/77(7)	7.2(0.9-59)*	4/73(6)	6.4(0.8-53)*
Severe incontinence	0/94(0)	1/93(1)	2.0(0.2-22)*	1/76(1)	2.5(0.2-27)*	1/73(1)	2.6(0.2-28)*
Moderate incontinence	24/94(26)	30/93(32)	1.3(0.8-2.0)	34/76(45)	**1.7(1.1-2.6)**	30/73(41)	1.5(0.97-2.3)
Lymphedema	0/94(0)	8/92(9)	**9.2(1.2-71)***	11/78(14)	**14(1.9-109)***	14/73(19)	**19(2.6-142)***
Numbness thigh/labia	3/90(3)	69/90(77)	**23(7.5-70)**	59/78(76)	**25(8.1-76)**	52/73(71)	**22(7.0-66)**
Not sexual active lately	41/91(45)	37/89(42)	0.9(0.7-1.3)	21/78(27)	0.6(0.4-0.9)	21/73(29)	0.6(0.4-1.0)
Little or no interest in sex	16/90(18)	25/90(28)	1.6(0.9-2.7)	20/78(26)	1.3(0.8-2.4)	18/73(25)	1.4(0.8-2.5)
Little or no lubrication during sexual arousal	3/80(4)	7/69(10)	2.7(0.7-10)	4/65(6)	2.0(0.5-8.2)	9/64(14)	**3.8(1.1-13)**
Dry vagina during coitus[a]	5/78(6)	9/55(16)	2.6(0.9-7.2)	10/60(17)	**3.1(1.1-8.2)**	13/55(24)	**4.6(1.7-12)**
Narrow or short vagina[a]	2/77(3)	10/55(18)	**7.0(1.6-31)**	9/59(15)	**5.9(1.3-26)**	14/55(25)	**9.9(2.4-42)**
Pain during coitus[a]	5/78(6)	8/55(15)	2.3(0.8-6.6)	11/59(19)	**3.1(1.2-8.4)**	10/55(18)	**2.9(1.0-9.7)**
No orgasm during coitus[a]	16/79(20)	18/58(31)	1.5(0.9-2.7)	18/60(30)	1.4(0.8-2.5)	18/55(33)	1.6(0.9-2.9)
No satisfaction with sex life	4/76(5)	8/66(12)	2.3(0.7-7.3)	11/62(18)	**3.3(1.1-10)**	13/58(22)	**4.3(1.5-12)**

Table 3. Prevalence and relative risk of micturation, defecation, lymphedema and sexual complaints after a radical hysterectomy with or without radiotherapy in a group of patients (n=94) before surgery compared to 3, 12 and 24 months after surgery. RR: relative risk; 95% CI:95% confidence interval. Bold numbers indicate significance at the 5% level. * Laplace succession rule. [a] This question was not answered when the women never had coitus.

Changes since the operation

We also calculated the change of all the sexual function items 24 months after the treatment (Table 4). Only the sexual activity had increased two years after the operation. All the other items deteriorated within 24 months of follow-up.

Change since operation (24 month) n 73	**Better %**	**No change %**	**Worse %**
Not sexually active	19	74	7
Little or no interest	12	62	26
Little or no lubrication	4	69	27
Dry vagina during coitus	4	66	30
Narrow/short vagina	4	64	32
Pain during coitus	8	66	26
No orgasm during coitus	11	63	26
Satisfaction sex life	8	55	37

Table 4. Change of all the sexual function items 24 months after the treatment (n=73).

Premenopausal versus postmenopausal

The ovaries were removed in 26 patients and 36 received radiotherapy. Analysis comparing premenopausal (i.e. women who stayed premenopausal and women who received HRT) versus postmenopausal women or women who became postmenopausal after the treatment, did show some differences. The absolute numbers, RR and corresponding 95% CI for all items are shown in Table 5. A significantly larger percentage of the patients who were postmenopausal before the treatment reported to be less sexually active lately and were less interested in sex compared to the women who were premenopausal. After the treatment a significantly larger percentage of the patients who were already postmenopausal before the treatment and the patients who became postmenopausal after the treatment, complained of no or less sexual activity and no or less interest in sex, up to 24 months follow-up. After 2 years follow-up only a significantly larger percentage of the patients who were postmenopausal after the treatment complained of a narrow or short vagina compared to the women who were premenopausal after the treatment. No other differences after 2 years follow-up were found.

Patient versus control

The absolute numbers, RR and corresponding 95% CI for all items are shown in Table 6.

After 3 and 12 months follow-up, a significantly larger percentage of patients reported diarrhoea and more problems with urge to urinate compared to women in the control group. After 2 years, the differences between the patients and controls concerning bladder dysfunction and colorectal motility disorders, were no longer statistically significant. Up to 2 years follow-up a significantly larger percentage of the patient group reported lymphedema than the control group.

	Before surgery		3 Months		12 Months		24 Months	
Characteristics	**pre**	**post**	**pre**	**post**	**pre**	**post**	**pre**	**post**
Often diarrhoea								
no./total no.(%)	1/77(1)	0/16(0)	1/57(2)	4/35(11)	2/49(4)	2/27(7)	1/47(2)	1/25(4)
RR pre- vs postmenopausal(95%CI)	1.0	2.3(0.2-24)*	1.0	6.5(0.8-56)	1.0	1.8(0.3-12)	1.0	1.9(0.1-29)
Often constipation								
no./total no.(%)	2/77(3)	1/16(6)	2/57(4)	1/35(3)	2/49(4)	1/27(4)	1/47(2)	1/25(4)
RR pre- vs postmenopausal(95%CI)	1.0	2.4(0.2-25)	1.0	0.8(0.1-8.7)	1.0	0.9(0.1-9.6)	1.0	1.9(0.1-29)
Little/no urge								
no./total no.(%)	0/77(0)	0/16(0)	6/57(11)	4/35(11)	3/49(6)	2/27(7)	3/47(6)	1/25(4)
RR pre- vs postmenopausal(95%CI)	1.0	4.6(0.3-70)*	1.0	1.1(0.3-3.6)	1.0	1.2(0.2-6.8)	1.0	0.6(0.1-5.7)
Severe incontinence								
no./total no.(%)	0/77(0)	0/16(0)	0/57(0)	1/35(3)	0/48(0)	1/27(4)	1/47(2)	0/25(0)
RR pre- vs postmenopausal(95%CI)	1.0	4.6(0.3-70)*	1.0	3.2(0.3-34)*	1.0	3.5(0.3-37)*	1.0	0.9(0.1-9.7)*
Moderate incontinence								
no./total no.(%)	18/77(23)	5/16(31)	20/57(35)	9/35(26)	20/48(42)	13/27(48)	18/47(38)	12/25(48)
RR pre- vs postmenopausal(95%CI)	1.0	1.3(0.6-3.1)	1.0	0.7(0.4-1.4)	1.0	1.2(0.7-1.9)	1.0	1.3(0.7-2.2)
Lymphedema								
no./total no.(%)	0/77(0)	0/16(0)	5/56(9)	3/35(9)	6/49(12)	5/28(18)	11/47(23)	3/25(12)
RR pre- vs postmenopausal(95%CI)	1.0	4.6(0.3-70)*	1.0	1.0(0.2-3.8)	1.0	1.5(0.5-4.4)	1.0	0.5(0.2-1.7)
Numbness thigh/labia								
no./total no.(%)	2/75(3)	1/14(7)	43/56(77)	26/33(79)	39/49(80)	20/28(71)	33/47(70)	18/25(72)
RR pre- vs postmenopausal(95%CI)	1.0	2.7(0.3-28)	1.0	1.0(0.8-1.3)	1.0	0.9(0.7-1.2)	1.0	1.0(0.8-1.4)
Not sexual active lately								
no./total no.(%)	29/74(40)	12/16(75)	14/56(25)	23/32(72)	7/49(14)	14/28(50)	8/47(17)	12/25(48)
RR pre- vs postmenopausal(95%CI)	1.0	**1.9(1.3-2.9)**	1.0	**2.9(1.7-4.8)**	1.0	**3.5(1.6-7.6)**	1.0	**2.8(1.3-6.0)**
Little or no interest in sex								
no./total no.(%)	7/74(10)	9/15(20)	10/56(18)	15/33(45)	5/49(10)	15/29(54)	7/47(15)	11/25(44)
RR pre- vs postmenopausal(95%CI)	1.0	**6.3(2.8-14)**	1.0	**2.6(1.3-5.0)**	1.0	**5.3(2.1-13)**	1.0	**3.0(1.3-6.7)**
Little or no lubriaction during sexual arousal								
no./total no.(%)	1/68(2)	2/11(2)	5/51(10)	2/17(12)	2/47(4)	2/17(12)	6/46(13)	3/17(18)
RR pre- vs postmenopausal(95%CI)	1.0	**12(1.2-125)**	1.0	1.2(0.3-5.6)	1.0	2.8(0.4-18)	1.0	1.4(0.4-4.8)
Dry vagina during coitus[a]								
no./total no.(%)	2/68(3)	3/9(33)	8/43(19)	1/11(9)	8/43(19)	2/16(13)	11/41(27)	2/13(8)
RR pre- vs postmenopausal(95%CI)	1.0	**11(2.2-59)**	1.0	0.5(0.1-3.5)	1.0	0.7(0.2-2.8)	1.0	0.6(0.2-2.3)
Narrow or short vagina[a]								
no./total no.(%)	1/68(2)	1/8(13)	7/43(16)	3/11(27)	6/43(14)	3/15(20)	6/41(15)	7/13(54)
RR pre- vs postmenopausal(95%CI)	1.0	8.5(0.6-123)	1.0	1.7(0.5-5.5)	1.0	1.4(0.4-5.0)	1.0	**3.4(1.4-8.5)**
Pain during coitus[a]								
no./total no.(%)	4/68(6)	1/9(11)	6/43(14)	2/11(18)	7/43(16)	4/15(27)	7/41(17)	3/13(23)
RR pre- vs postmenopausal(95%CI)	1.0	1.9(0.2-15)	1.0	1.3(0.3-5.6)	1.0	1.6(0.6-4.8)	1.0	1.4(0.4-4.5)
No orgasm during coitus[a]								
no./total no.(%)	11/68(16)	5/10(50)	13/44(30)	5/13(39)	9/43(21)	8/16(50)	11/41(27)	6/13(46)
RR pre- vs postmenopausal(95%CI)	1.0	**3.1(1.4-7.0)**	1.0	1.3(0.6-3.0)	1.0	2.4(1.1-5.1)	1.0	1.7(0.8-3.7)
Not content with sex life								
no./total no.(%)	2/68(3)	2/7(29)	3/48(6)	5/17(29)	7/46(15)	4/15(27)	10/43(23)	3/14(21)
RR pre- vs postmenopausal(95%CI)	1.0	**9.7(1.6-58)**	1.0	**4.7(1.3-18)**	1.0	1.8(0.6-5.2)	1.0	0.9(0.3-2.9)

Table 5. Age adjusted relative risks of colorectal motility disorders, bladder dysfunction, lymphedema and sexual dysfunction. Premenopausal (n=77) versus postmenopausal (n=16). RR: relative risk; 95% CI:95% confidence interval. Bold numbers indicate significance at the 5% level. * Laplace succession rule. [a] This question was not answered when the women never had coitus. Pre, premenopausal; post, postmenopausal.

No/total no.responding (%)		Before surgery		3 Months		12 Months		24 Months	
Characteristics	**Control**	**Patient**	**RR(95%CI)**	**Patient**	**RR(95%CI)**	**Patient**	**RR(95%CI)**	**Patient**	**RR(95%CI)**
Often diarrhoea	2/223(1)	1/94(1)	1.2(0.1-13)	5/93(5)	**6.0(1.2-30)**	4/77(5)	**5.8(1.1-31)**	2/73(3)	3.1(0.4-21)
Often constipation	5/223(2)	3/94(3)	1.4(0.4-5.8)	3/93(3)	1.4(0.4-5.9)	4/77(5)	2.3(0.6-84)	3/73(4)	1.8(0.5-7.5)
Little/no urge	4/223(2)	0/93(0)	0.5(0.1-4.0)*	10/93(11)	**6.0(1.9-19)**	5/77(7)	**3.6(1.0-13)**	4/73(6)	3.1(0.8-12)
Severe incontinence	0/224(0)	0/94(0)	2.4(0.2-37)*	1/93(1)	4.8(0.4-52)*	1/76(1)	5.8(0.5-64)*	1/73(1)	6.2(0.6-67)*
Moderate incontinence	75/224(33)	24/94(26)	0.8(0.5-1.1)	30/93(32)	1.0(0.7-1.4)	34/76(45)	1.3(0.98-1.8)	30/73(41)	1.2(0.9-1.7)
Lymphedema	7/224(3)	0/94(0)	0.3(0.0-2.3)*	8/92(9)	**2.8(1.0-7.5)**	11/78(14)	**4.5(1.8-11)**	14/73(19)	**6.1(2.6-15)**
Numbness thigh/labia	2/223(1)	3/90(3)	3.7(0.6-22)	69/90(77)	**86(21-341)**	59/78(76)	**84(21-337)**	52/73(71)	**79(20-318)**
Not sexual active lately	37/224(17)	41/91(45)	**2.7(1.9-4.0)**	37/89(42)	**2.5(1.7-3.7)**	21/78(27)	**1.6(1.0-2.6)**	21/73(29)	**1.7(1.1-2.8)**
Little or no interest in sex	16/222(7)	16/90(18)	**2.5(1.3-4.7)**	25/90(28)	**3.9(2.2-6.9)**	20/78(26)	**3.6(1.9-6.5)**	18/73(25)	**3.4(1.8-6.4)**
Little or no lubrication during sexual arousal	6/213(3)	3/80(4)	1.3(0.3-5.2)	7/69(10)	**3.6(1.3-10)**	4/65(6)	2.2(0.6-7.5)	9/64(14)	**5.0(1.9-14)**
Dry vagina during coitus[a]	8/195(4)	5/78(6)	1.6(0.5-4.6)	9/55(16)	**4.0(1.6-10)**	10/60(17)	**4.1(1.7-9.8)**	13/55(24)	**5.8(2.5-13)**
Narrow or short vagina[a]	4/196(2)	2/77(3)	1.3(0.2-6.8)	10/55(18)	**8.9(2.9-27)**	9/59(15)	**7.5(2.4-23)**	14/55(25)	**13(4.3-36)**
Pain during coitus[a]	3/196(2)	5/78(6)	**4.2(1.0-17)**	8/55(15)	**9.5(2.6-35)**	11/59(19)	**12(3.5-42)**	10/55(18)	**12(3.4-42)**
No orgasm during coitus[a]	41/196(21)	16/79(20)	1.0(0.6-1.6)	18/58(31)	1.5(0.9-2.4)	18/60(30)	1.4(0.9-2.3)	18/55(33)	1.6(0.98-2.5)
No satisfaction with sex life	6/202(3)	4/76(5)	1.8(0.5-6.1)	8/66(12)	**4.1(1.5-11)**	11/62(18)	**6.0(2.3-15)**	13/58(22)	**7.6(3.0-19)**

Table 6. Prevalence and relative risk of micturation, defecation, lymphedema and sexual complaints after a RHL with or without radiotherapy in a group of patients (n=94) compared to age matched control women from the general population (=224), 3, 12 and 24 months after surgery. RR: relative risk; 95% CI:95% confidence interval. Bold numbers indicate significance at the 5% level. * Laplace succession rule. [a] This question was not answered when the women never had coitus.

Before the operation, a significantly larger percentage of the patients reported to be not sexually active lately, to have little or no interest in sex, and having more pain during coitus compared to the control group. Throughout the 2 years follow-up, this statistical significance persisted. Little or no lubrication during sexual arousal was reported by a significantly larger percentage of the patients after 3 and 24 months. A dry vagina during coitus, a narrow or short vagina and numb areas around the labia all significantly increased throughout the first 2 years after the treatment. The percentage of patients who complained of no orgasm during coitus was never statistically significant. A significantly larger percentage of the patients reported dissatisfaction with their sex life compared to the controls up to 2 years of follow-up.

Radiotherapy versus no radiotherapy

We compared the patients with adjuvant pelvic radiotherapy to the patients without adjuvant pelvic radiotherapy. Thirty-six of the 94 patients received adjuvant radiotherapy after surgery. The absolute numbers, RR and corresponding 95% CI for all items are shown in Table 7.

When compared to surgery alone, the patients with adjuvant pelvic radiotherapy were not more often significantly associated with bladder dysfunction, colorectal motility dysfunction or lymphedema. Only

	Before surgery		3 Months		12 Months		24 Months	
Characteristics	**no RT**	**RT**	**no RT**	**RT**	**no RT**	**RT**	**no RT**	**RT**
Often diarrhoea								
no./total no.(%)	1/58(2)	0/36(0)	0/58(0)	5/35(14)	1/48(2)	3/29(10)	0/47(0)	2/26(8)
RR RT vs surgery alone(95%CI)	1.0	0.8(0.1-8.5)*	1.0	**10(1.3-80)***	1.0	5.0(0.5-46)	1.0	5.3(0.6-49)*
Often constipation								
no./total no.(%)	0/58(0)	3/36(8)	2/58(3)	1/35(3)	2/48(4)	2/29(7)	3/47(6)	0/26(0)
RR RT vs surgery alone(95%CI)	1.0	6.4(0.7-55)*	1.0	0.8(0.1-8.8)	1.0	1.7(0.3-11)	1.0	0.4(0.1-3.8)*
Little/no urge								
no./total no.(%)	0/57(0)	0/36(0)	5/58(9)	5/35(14)	1/49(2)	4/28(14)	1/47(2)	3/26(12)
RR RT vs surgery alone(95%CI)	1.0	1.6(0.1-24)*	1.0	1.7(0.5-5.3)	1.0	7.0(0.8-60)	1.0	5.4(0.6-50)
Severe incontinence								
no./total no.(%)	0/58(0)	0/36(0)	0/58(0)	1/35(3)	0/49(0)	1/27(4)	0/47(0)	1/26(4)
RR RT vs surgery alone(95%CI)	1.0	1.6(0.1-25)*	1.0	2.3(0.3-35)*	1.0	3.6(0.3-38)*	1.0	3.6(0.3-37)*
Moderate incontinence								
no./total no.(%)	11/58(19)	13/36(36)	20/58(35)	10/35(29)	18/49(37)	16/27(59)	18/47(38)	12/26(46)
RR RT vs surgery alone(95%CI)	1.0	1.9(0.96-3.8)	1.0	0.8(0.4-1.6)	1.0	**1.6(1.0-2.6)**	1.0	1.2(0.7-2.1)
Lymphedema								
no./total no.(%)	0/58(0)	0/36(0)	4/57(7)	4/35(11)	4/49(8)	7/29(24)	8/47(17)	6/26(23)
RR RT vs surgery alone(95%CI)	1.0	1.6(0.1-25)*	1.0	1.6(0.4-6.1)	1.0	3.0(0.95-9.2)	1.0	1.4(0.5-3.5)
Numbness thigh/labia								
no./total no.(%)	1/56(2)	2/34(6)	48/57(84)	21/33(64)	39/49(80)	20/29(69)	36/47(77)	16/26(62)
RR RT vs surgery alone(95%CI)	1.0	3.2(0.3-35)	1.0	0.8(0.6-1.0)	1.0	0.9(0.7-1.2)	1.0	0.8(0.6-1.1)
Not sexual active lately								
no./total no.(%)	25/56(45)	16/35(46)	18/57(32)	19/32(59)	11/49(22)	10/29(35)	10/47(21)	11/26(42)
RR RT vs surgery alone(95%CI)	1.0	1.0(0.6-1.6)	1.0	**1.9(1.2-3.0)**	1.0	1.5(0.8-3.2)	1.0	2.0(0.98-4.0)
Little or no interest in sex								
no./total no.(%)	7/56(13)	9/34(27)	14/57(25)	11/33(33)	10/49(20)	10/29(35)	9/47(19)	9/26(35)
RR RT vs surgery alone(95%CI)	1.0	2.1(0.9-5.2)	1.0	1.4(0.7-2.6)	1.0	1.7(0.8-3.6)	1.0	1.8(0.8-4.0)
Little or no lubriaction during sexual arousal								
no./total no.(%)	1/51(2)	2/29(7)	4/48(8)	3/21(14)	2/44(5)	2/21(10)	6/43(14)	3/21(14)
RR RT vs surgery alone(95%CI)	1.0	3.5(0.3-37)	1.0	1.7(0.4-7.0)	1.0	2.1(0.3-14)	1.0	1.0(0.3-3.7)
Dry vagina during coitus[a]								
no./total no.(%)	3/50(6)	2/28(7)	7/41(17)	2/14(14)	5/40(13)	5/20(25)	9/38(24)	4/17(24)
RR RT vs surgery alone(95%CI)	1.0	1.2(0.2-6.7)	1.0	0.8(0.2-3.6)	1.0	2.0(0.7-6.1)	1.0	0.1(0.4-2.8)
Narrow or short vagina[a]								
no./total no.(%)	2/49(4)	0/28(0)	5/41(12)	5/14(36)	5/40(13)	4/19(21)	7/38(18)	7/17(41)
RR RT vs surgery alone(95%CI)	1.0	0.6(0.1-5.3)*	1.0	2.9(0.99-8.6)	1.0	1.7(0.5-5.6)	1.0	2.2(0.93-5.4)
Pain during coitus[a]								
no./total no.(%)	4/50(8)	1/28(4)	6/41(15)	2/14(14)	6/40(15)	5/19(26)	6/38(16)	4/17(24)
RR RT vs surgery alone(95%CI)	1.0	0.5(0.1-3.8)	1.0	1.0(0.2-4.3)	1.0	1.8(0.7-5.0)	1.0	1.5(0.5-4.6)
No orgasm during coitus[a]								
no./total no.(%)	8/50(16)	8/29(28)	12/42(29)	6/16(38)	11/40(28)	7/20(35)	12/38(32)	6/17(35)
RR RT vs surgery alone(95%CI)	1.0	1.7(0.7-4.1)	1.0	1.3(0.6-2.9)	1.0	1.3(0.6-2.8)	1.0	1.1(0.5-2.5)
Not content with sex life								
no./total no.(%)	3/51(6)	1/25(4)	3/44(7)	5/22(23)	8/42(19)	3/20(15)	11/41(27)	2/17(12)
RR RT vs surgery alone(95%CI)	1.0	0.7(0.1-6.2)	1.0	3.3(0.9-13)	1.0	0.8(0.2-2.7)	1.0	0.4(0.1-1.8)

Table 7. Age adjusted relative risks of colorectal motility disorders, bladder dysfunction, lymphedema and sexual dysfunction. Radiotherapy (n=36) versus no radiotherapy (n=58). RR: relative risk; 95% CI:95% confidence interval. Bold numbers indicate significance at the 5% level. *Laplace succession rule. [a] This question was not answered when the women never had coitus. RT, radiotherapy.

at 3 months follow-up, a significantly larger percentage of patients with adjuvant pelvic radiotherapy experienced more often diarrhoea and at 12 months follow-up moderate urine incontinence (Table 7).

After 3 months a significantly larger percentage of patients with adjuvant pelvic radiotherapy were less sexually active lately compared to the patients without adjuvant radiotherapy. No significant differences in the percentages were found between the two patient groups for numb areas around the labia, dry vagina, pain during coitus, narrow vagina, little or no lubrication, sexual activity, interest in sex, satisfaction with sex life, and orgasm (Table 7).

Discussion

The current study shows that treatment for cervical cancer stage I-IIa by RHL with or without adjuvant pelvic radiotherapy has a negative effect on sexual function. The difference in sexual function was not only significant compared to the controls but also compared to the sexual situation before the treatment. The changes or problems included less lubrication, a narrow and short vagina, numb areas around the labia, dyspareunia and sexual dissatisfaction. Furthermore, in the long term no differences were observed for bladder and colorectal dysfunction.

Retrospective studies of frequency of late postoperative micturition and colorectal problems show various figures: incontinence in 10-12%, urinary retention or inability to void in 2-4% and severe constipation in 5-10% (6;10;26;27). After 2 years follow-up, we found no significant difference anymore concerning bladder dysfunction and colorectal dysfunction compared to the control group and compared to the situation before surgery. Contrary to these findings, Sood et al.(31), for example, have shown that anorectal manometry revealed significant changes in colorectal function after RHL, showing a pattern which correlates to a partial denervation of the bowel (31). Furthermore, results of urodynamic studies evaluating urinary dysfunction in patients after RHL are suggestive for disruption of the autonomic nerve supply to the bladder and urethra (8;9). The fact that the patients in our study did not report a significant difference in bladder and colorectal functions 24 months after the operation compared with the situation before the operation might be a reflection of post-surgical recovery or an indication that the perception of quality of life may be independent of there objective measures. The relief resulting from the completion of this potentially curative treatment may also have contributed to the subjective improvement despite changes in bowel and bladder function. And finally, most studies of colorectal and micturial dysfunction offer data collected from the medical files (6;10;26;27). This study used questionnaires and has a longitudinal design what makes it more difficult to compare with the literature.

In the literature, secondary lymphedema after RHL is reported up to 23% (28;29). We found percentages of up to 19%. As well as compared to the control group as compared to the situation before the operation, a significantly larger percentage of the patients complained of lymphedema up to 24 months of follow-up.

As to the short-term effects of RHL on sexual function, Grumann et al. (21) assessed in a study of 20 women with early stage cervical carcinoma the effects of RHL on the sexual function up to 8 months. They found that women with cancer had vaginal dryness 4 and 8 months after the operation and reduced sexual activity. Modest but consistent downward trends regarding sexual activity, sexual desire, excitement, orgasm, and resolution were found 4 and 8 months after surgery, although these last items were not statistically significant (21). Jensen et al. also found short-term adverse effects on sexual function: dyspareunia, short vagina and sexual dissatisfaction (5). In line with these results, we also found that during the first months after the operation women with early stage cervical cancer have sexual dysfunction.

Concerning the long-term effects, Butler-Manual found in a retrospective survey of women who had undergone RHL with or without radiotherapy a significant increase of vaginal dryness during sexual activity and dissatisfaction with their sexlife (16). In their cross-sectional study, Bergmark et al. compared 256 women with a history of early stage cervical cancer with 350 controls using validated questionnaires. They found that the patients had decreased lubrication, genital swelling during arousal, and a short vagina during intercourse (3). The long-term effects that Jensen et al. reported were complaints that persisted after 2 years and included less vaginal lubrication and sexual interest (5). We also find these long-term effects on sexual function. The short term effects described above by Jensen et al., still persisted after 2 years follow-up in the current study. In agreement with these authors it can be concluded that up to 2 years after the RHL, women with early stage cervical cancer experience negative effects on sexual function.

In the current study, 38% received radiotherapy after the operation. A significantly larger percentage of patients with adjuvant radiotherapy were less sexually active and had more diarrhoea after 3 months follow-up. At 12 months follow-up, a significantly larger percentage of patients with adjuvant radiotherapy had moderate incontinence. But adjuvant radiotherapy did not increase the risk of bladder dysfunction, colorectal motility disorders, lymphedema and other sexual functions after 2 years follow-up.

One would expect that hormonal status particularly influences the sexual functioning, because castration lowers serum testosterone and estrogens concentrations (3). In line with this, the current study showed that up to 2 years follow-up women who were postmenopausal or became postmenopausal had less libido and were less sexually active compared to the women who were premenopausal. However, Bergmark et al. suggested that ovarian hormones have minor effects on libido or the frequencies of sexual intercourse (3). In the current study, a significantly larger percentage of the patients who were postmenopausal after the treatment reported a narrow or short vagina after 2 years follow-up. Most patients who became postmenopausal after the treatment had received adjuvant radiotherapy. Although adjuvant radiotherapy did not show an increase risk on sexual function, a short or narrow vagina is an effect of the adjuvant radiotherapy and not due to hormonal changes directly (20). This could explain the difference that a significantly larger percentage of the patients who were postmeno-

pausal after the treatment reported a narrow or short vagina compared to the premenopausal patients. Other significant differences were not found. We suggest that the hormonal status has less effect on complaints as pain during coitus, less lubrication and orgasm.

Autonomic nerve damage during surgery is thought to play a crucial role in the aetiology of bladder dysfunction, colorectal motility disorders and sexual dysfunction that can be seen after RHL. The autonomic nerves are essential for a normal physiologic function and neurogenic control of the pelvic organs (11;22;26;27;30-32). The autonomic nerves for example, supply the blood vessels of the internal genitalia and are involved in the neural control of vasocongestion and, consequently, lubrication swelling response (32). Evidence from surgical practice has shown that a lesser extent of surgically inflicted autonomic nerve injury lowers the incidence of morbidity (33-36).

In our centre, we used photoplethysmographic assessment of vaginal pulse amplitude to measure objectively the vaginal blood flow during sexual arousal (30;37). Increased vaginal blood flow during sexual arousal reflects a highly automatized genital response mechanism, occurring irrespectively of subjective appreciation of the sexual stimulus (38;39). From this study, it was concluded that a RHL seems to be associated with a disturbed vaginal blood flow response during sexual arousal caused by denervation of the vagina (40).

The surgical concept of the identification and preservation of the pelvic autonomic nerves was introduced by Japanese gynaecologists in the sixties (36). Recently, the Leiden Medical Centre developed a nerve-sparing technique that is described elsewhere (11). This technique was not yet utilized in the present study and the benefit of this procedure will be studied in a multicentre prospective trial in order to establish the results of nerve-sparing surgery and the effects on sexual functioning.

The current study did show sexual dysfunction after treatment for low stage cervical carcinoma. It is the first longitudinal study of self-reported bladder, defecation, sexual and vaginal problems with a baseline score before the RHL. We compared the morbidity after treatment with the situation before treatment and the normal population. As could be expected, before the operation a significantly larger percentage of the patients reported not to be sexually active, have little or no interest in sex and have more pain during coitus, compared to the healthy controls. Probably this has to do with their disease status itself or with the psychological impact of the illness. Psychological function and quality of life status effect sexual function in women (41). Future research on the effect of RHL should therefore include self-report measures of sexual functioning as well as of depression, anxiety and quality of life issues including relationship parameters. The control group consisted of employees from the hospitals and relatives and friends of these employees, who had not undergone a hysterectomy in the past. Although the control group was not an a-select sample of the Dutch general population, the control group was matched for age, as this is related to sexual function (41). We used the Gynaecologic Leiden Questionnaire, which is the first developed Dutch questionnaire consisting of the items for sexual dysfunction, voiding- and bowel problems for women with cancer.

This study has an observational design. Despite this, we conclude that RHL for the treatment of early stage cervical carcinoma is associated with adverse effects mainly on sexual functioning. Adjuvant radiotherapy after RHL seemed not to be a major factor contributing to the complaints, in the present study. Whether or not the nerve sparing technique will lead to lower morbidity with comparable treatment results will have to be established.

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