Sexual functioning after treatment for testicular cancer

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Comparison of Treatment Modalities

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BACKGROUND. This retrospective study evaluates changes in sexual functioning after treatment for testicular cancer and investigates whether there is a relationship with different treatment modalities.

METHODS. A self-reported questionnaire was sent to 337 men who had been treated for testicular cancer at the University Hospital Groningen between 1977 and 1994. Medical information was obtained from the patient records.

RESULTS. A response was received from 287 men (85%); 264 patients were included in this study (78%). The mean patient age at follow-up was 37.7 years (range, 17–71 years). The mean follow-up period was 6.7 years (range, 0.25–18 years). Decrease in sexual functions was reported by 40% of patients (decrease in libido: 19%; arousal: 12% erection: 12.5%; orgasm: 19%; and ejaculation: 26%). Moreover, 23.5% of patients responding reported decreased sexual activity and 12.5% were dissatisfied with their sexual functioning. Patients with Stage II–IV nonseminoma who had been treated with polychemotherapy (PCT) with or without resection of residual retroperitoneal tumor mass (RRRTM) (PCT ± RRRTM) reported a significantly sharper decrease in sexual functioning than patients who had been followed with a wait-and-see policy (W & S) (Stage I nonseminoma patients). It was noteworthy that patients treated by PCT alone reported more sharply decreased sexual functioning than patients treated by PCT + RRRTM. Patients treated by radiotherapy (Stage I–IIA seminoma) did not report findings significantly different from the W & S group.

CONCLUSIONS. Testicular cancer patients are at risk for reduced sexual functioning, especially when treated by chemotherapy, with or without resection of residual tumor. Although chemotherapy may influence somatic aspects of sexual functioning, it appears that psychologic factors arising from the confrontation with testicular cancer play a strongly mediating (if not determining) role. ***Cancer* 1997;80:454–64.** © *1997 American Cancer Society.*

KEYWORDS: testis, testicular cancer, sexual functioning, sexuality, treatment, self-report questionnaire.

Although testicular cancer is a rare form of cancer, there is an increasing incidence in the industrialized countries and it is one of the most common malignancies among young men.[1,2] The tumor is found chiefly in young men between the ages of 25 and 35 years, their most sexually active years. The incidence in the Netherlands is 4.7 per 100.000 population.[3] It is important to evaluate the extent to which sexual and fertility problems occur, because nearly 90% of these patients can (often after intensive treatment) be cured completely.[4]

Within the field of oncology there is increasing attention being paid to sexual problems resulting from illness and the associated

treatment modalities.[5–10] In testicular cancer patients, much attention has been focused on the possible physiologic consequences on overt sexual behavior (erection, coitus, and ejaculation). It is only during the past decade that the evaluation of sexuality in terms of its more subjective aspects (libido, arousal, orgasm, and satisfaction)[11–13] have entered the discussion.[14–22]

Data on sexual functioning after treatment for testicular cancer vary widely and only a few studies analyzed the results of sexual functioning in connection with the treatment applied.[14,15,18–20,22,23] However, comparison of outcomes is difficult due to lack of conformity regarding treatment regimens, composition of the patient groups, and research questions in the various studies. For example, in some studies, a major risk factor for sexual dysfunction was found to be irradiation; [18–20,22] in others it was found to be chemotherapy.[15,23,24] Some studies assume that there are no differences between different treatment groups.[14,25] One study found no differences between irradiated patients when compared with patients under surveillance only, but found significant differences when these same patients were compared with healthy controls,[20] whereas in another study there were no significant differences between patients under surveillance and healthy controls.[26] Therefore, it is not quite clear whether and to what extent physiologic consequences of a particular treatment, or emotional and cognitive consequences, influence sexual functioning.

To gain better insight into possible changes in the subjective experience of sexuality after testicular cancer, as well as the influence of various treatment modalities, a study was performed on patients who were treated for testicular cancer at the University Hospital Groningen between 1977–1994. In this study, the following two questions played a central role: 1) To what extent does testicular cancer and/or its treatment lead to changes in sexual functioning; and 2) To what extent are there differences in sexual functioning after treatment between the various treatment groups.

Treatment-Related Biologic-Organic Influences on Sexual Functioning

To examine the extent to which biologic-organic aspects relevant to sexual functioning may become disturbed after treatments for testicular cancer, an extensive search of the literature was performed on the possible hormonal, vascular, or neurologic changes.[27]

After unilateral orchidectomy, decreased testosterone levels were found in 5–34% of patients, probably due to preexisting abnormalities in the remaining testicle.[28–31] However, normal sexual functioning is possible even with very low serum testosterone levels (6–12 nmol/L),[32,33] and it has been shown that erection can still occur even after castration.[34,35] The exact consequences of subnormal testosterone levels on orgasm and ejaculation are current topics of discussion.[32,36,37] Radiotherapy (RT) may decrease Leydig cell functioning in the remaining testicle[38–40] or testosterone production.[41,42] Although the penile blood vessels lie outside the radiation field, erectile dysfunction may be related to radiation damage to the small blood vessels and nerves that regulate the penile blood supply.[43–45] Polychemotherapy (PCT) may decrease testosterone levels through Leydig cell damage within the remaining testicle,[43] or by hyperprolactinemia.[46] However, Leydig cell dysfunction probably is temporary.[47] Erectile dysfunction may be related to PCT-induced vascular damage.[16,48–50] In addition, theoretically, decreased ejaculation, erectile dysfunction, or orgasmic difficulties may also be related to PCT-induced peripheral neuropathy.[16,49]

In patients treated by resection of residual retroperitoneal tumor mass after PCT (PCT+RRRTM), 6–30% reported ejaculatory disturbances.[51–55] It is unknown whether retrograde ejaculation has a negative influence on the intensity of orgasm.[56] In the case of reduced orgasmic intensity in patients treated by PCT and RRRTM, it is most likely not the retrograde ejaculation, but PCT that is responsible.[24,57] Because the parasympathetic nerve tracts that regulate erection lie outside the area of RRRTM, the same may be true in the case of erectile disturbances after PCT+RRRTM.

METHODS

Patients and Treatments

All patients who had been treated for a malignant testicular germ cell tumor between 1977–1994 at the University Hospital Groningen and who were still alive, were approached by means of a written questionnaire (n = 337). The patients were informed about the use of the data by a cover letter wherein it was emphasized that nonresponse would not affect treatment. On a separate form patients could indicate whether they wished to receive information about the results of the study. Permission to perform the study had been obtained from the Medical Ethical Committee.

Two histologic types of testicular tumor were distinguished: seminoma (ST) and nonseminomatous germ cell tumors (NSGCT); ST is generally diagnosed at a later age (40–50 years) than NSGCT. Patients were staged according to the Royal Marsden Hospital Staging Classification,[58] as follows: Stage I: no metastases evident outside testis; Stage II: infradiaphragmatic lymph node metastasis (IIA: < 2 cm; IIB: 2–5 cm; and IIC: > 5 cm); Stage III: supradiaphragmatic lymph node metastases (A, B, and C, as for Stage II); and Stage

IV: extranodal metastases (abdominal status same as for Stage II).

All patients underwent orchidectomy. Patients with Stage I NSGCT were treated by orchidectomy alone and entered an intense outpatient follow-up policy (''Wait & See'' [W&S]), which was comprised of physical check-ups, screening for elevated tumor markers, and computed tomography scanning.[59] Patients with metastasized NSGCT (Stage II–IV) received four induction courses of PCT: cisplatin in combination with vinblastine and bleomycin (PVB), or with etoposide rather than vinblastine (BEP).[60] At the University Hospital Groningen, PCT has been used since 1976.[61,62] If there was any residual retroperitoneal tumor tissue, surgical resection was subsequently undertaken.[53,63] Patients with Stage I or IIA ST received RT in a dose of 25–30 grays (Gy) to the ipsilateral paraaortal and parailiac lymph nodes.[64,65] Patients with Stage IIB–IV ST also received four courses of PVB or BEP, but without additional surgical intervention.

Design

From a medical point of view, treatment with the W&S approach is not as far-reaching as that within the other treatment approaches; after orchidectomy, the patients only have to attend regular outpatient check-ups. Therefore, to evaluate the possible influence of the treatment modality (RT, PCT, or PCT+RRRTM), the W&S group formed a very acceptable control group.

Questionnaire

Because there were no adequate validated questionnaires available, a questionnaire was designed in which patients could indicate the extent to which they felt their sexual functioning had changed after treatment for testicular cancer. Questions concerned: decrease of sexual response (libido, sexual arousal, erection, and orgasm) decrease, absence, retarded, or premature ejaculation; decrease in sexual satisfaction; changes in sexual activities; and changes in the value of sexuality because of testicular cancer and its treatment.

In addition, there were questions regarding demographic variables (age, relationship, education, religion, and work) and patients were asked if there were any other physical abnormalities besides testicular cancer. The questionnaire comprised a total of 31 items. Data on the independent variables (tumor type: NSGCT/ST, and treatment [W&S, RT, PCT, and PCT+RRRTM]) were obtained from the medical records.

Scoring

Changes in sexual response functions and sexual satisfaction could be indicated on a 4-point scale (score of 0: ''no change at all'' to score of 3: ''sharp decrease''). Ejaculatory problems could be indicated as early, late, decreased, or completely absent. Changes in sexual activity were measured by combining the questions on sexual activity before the diagnosis and currently; in this way, a 7-point scale was obtained, from ''sharp decrease''(score of −3) to ''sharp increase''(score of +3). Changes in the value of sexuality could be indicated on a 5-point scale, from ''has become far less important''(score of −2) to ''has become much more important'' (score of +2).

Statistical Analysis

To portray the clinical relevance of the results in interpretive percentages, the raw scores for the above-mentioned dependent variables were combined. Four-point scales were dichotomized into two categories: scores 0 and 1 (no change and slight change), and scores 2 and 3 (moderate change and sharp change) were taken together. Because premature or retarded ejaculation was indicated by only 13 patients (5%) the results of these items are described briefly, but not used in analyses. To obtain comparable outcomes, reduced ejaculation was scored as 2 and complete absence was scored as 3. Variables for which the patient was asked to indicate the amount of change were reduced to three categories: decrease, no change, and increase in the relevant aspect.

To present the average outcomes of the various scales in a comparable manner, the raw scores were standardized on a scale from 0 to 10. To analyze the differences between the various treatment groups, means and standard deviations (SD) of the raw scores were used (chi square- or Mann-Whitney U test for categoric variables, and Student's t or analysis of variance [ANOVA] for continuous variables.) A P value $\leq$ 0.05 was considered to be significant. Correlations were calculated using Spearman's Rho.

RESULTS

Response

The questionnaire was returned by 287 patients (response rate, 85%). Those who did not have complete medical data (n = 9; 2.7%), or who underwent no standard treatment (n = 5; 1.5%), or had bilateral testicular cancer (n = 9; 2.7%) were excluded. A total of 264 patients (78%) remained for further analysis.

Patient Characteristics

Table 1 provides an overview of the patient characteristics (n = 264; 78%). There were no significant differ-

TABLE 1
Patient and Treatment Characteristics (n = 264)

	Total (n = 264) (100%)	W & S (n = 59) (22.5%)	RT (n = 41) (15.5%)	PCT (n = 42) (16%)	PCT + RRRTM (n = 122) (46%)	Significant *P* value
Age, yrs (SD)	37.7 (9.7)	34.2 (9.8)	43.4 (10.5)	38.9 (9.8)	36.9 (8.5)	0.0001[a]
Follow-up, yrs (SD)	6.7 (4.4)	4.4 (3.2)	3.8 (2.2)	7.1 (3.5)	8.7 (4.6)	0.0000[a]
Partner (%)						
No	28 (10.5)	5 (8.5)	5 (12)	5 (12)	13 (11)	
Yes	236 (89.5)	54 (91.5)	36 (88)	37 (88)	109 (89)	NS[b]
Work (%)						
No	21 (8)	5 (8.5)	7 (17.5)	2 (5)	7 (5.5)	
Yes	219 (83)	49 (83)	28 (68)	35 (83)	107 (88)	
Other	24 (9)	5 (8.5)	6 (14.5)	5 (12)	8 (6.5)	NS[b]
Education (%)						
Lower	64 (24)	17 (29)	10 (24.5)	9 (21.5)	28 (23)	
Middle	133 (50.5)	28 (47)	16 (39)	28 (66.5)	61 (50)	
High	67 (25.5)	14 (24)	15 (36.5)	5 (12)	33 (27)	NS[b]
Religion (%)						
No	161 (61)	42 (71)	28 (68)	24 (57)	67 (55)	NS[b]
Yes	103 (39)	17 (29)	13 (32)	18 (43)	55 (45)	
Other diseases (%)						
No	216 (82)	53 (90)	32 (78)	32 (76)	99 (81)	NS[b]
Yes	48 (18)	6 (10)	9 (22)	10 (24)	23 (19)	

W & S: intensive regular outpatient check-ups (Wait & See); RT: radiotherapy; PCT: polychemotherapy; RRRTM: resection of residual retroperitoneal tumor mass; NS: not significant; SD: standard deviation.
[a] Determined by analysis of variance.
[b] Determined by chi-square test; NS where $P > 0.05$.

ences in mean age and mean follow-up between individuals included and not included (n = 23; 6.8%) and nonrespondent patients (n = 27; 8%) Of a total of 264 patients, 59 had Stage I NSGCT with the W&S policy (22.5%), 41 had ST and were followed by 25–30 Gy adjuvant RT(15.5%), 42 had a disseminated NSGCT and were treated by PCT (16%), and another 122 PCT patients received adjuvant surgery (PCT+RRRTM; 46%). At the time of the study, the mean age of the total patient group was 37.7 years (range, 17–71 years; SD, 9.7 years). The mean age of the patients treated with RT (all ST) was 43.4 years, which was 9 years older than the mean age of the W&S group (34.2 years). The four treatment groups differed significantly in mean age ($P = 0.0001$). The mean follow-up period was 6.7 years (range, 0.25–17.7 years; SD, 4.4 years); the 4 groups differed significantly on this aspect ($P = 0.0000$). The mean follow-up period in the W&S group (4.4 years) was much shorter compared with the PCT group (7.1 years) and the PCT+RRRTM group (8.7 years). This can be explained by the fact that approximately 25% of patients originally in the W&S group developed metastases during follow-up and subsequently received PCT.[59] The majority of patients had a partner (n = 236; 89.5%) and were employed (n = 219; 83%), there were no significant differences between the 4 treatment groups with regard to these and other demographic variables. Other diseases in addition to testicular cancer were reported by 48 patients (18%); there were no significant differences between the 4 treatment groups, although the W&S group reported the fewest number of patients with other diseases (n = 6; 10%) than the other groups (RT: n = 9; 22%; PCT: n = 10; 24%; and PCT+RRRTM: n = 23; 19%). The diseases most frequently mentioned by the patients were: back pain (four times), stomach complaints (four times), Peyronie's disease (two times), cardiac problems (two times), and general fatigue (two times).

Changes in Sexual Functioning in the Total Patient Group

Table 2 provides information about the reported incidence of posttreatment decreased sexual response (libido [a], arousal [b], erection [c], and orgasm [d]), decreased ejaculation (e), and sexual dissatisfaction (f), as well as changes in sexual activity (g) and the value of sexuality (h). Libido loss was reported by 51 patients (19%), reduced arousal by 32 (12%), reduced erection by 33 (12.5%), and reduced orgasm by 50 (19%). Retarded ejaculation was mentioned by only one patient from the PCT+RRRTM group, premature ejaculation was reported overall by 12 patients (total group: 4.5%: W&S: 5%; RT: 5%; PCT: 7%;

TABLE 2
Changes in Sexual Functioning (Raw Scores Classified into Percentages) (n = 264)

	Total (n = 264) No. (%)	W & S (n = 59) No. (%)	RT (n = 41) No. (%)	PCT (n = 42) No. (%)	PCT + RRRTM (n = 122) No. (%)
a. Libido decreased	51 (19)	7 (12)	9 (22)	13 (29.5)	23 (19)
b. Arousal decreased	32 (12)	3 (5)	7 (17)	6 (14.5)	16 (13)
c. Erection decreased	33 (12.5)	2 (3.5)	6 (14.5)	7 (17)	18 (15)
d. Orgasm decreased	50 (19)	7 (12)	6 (14.5)	12 (28.5)	25 (20.5)
e. Ejaculate: decreased	37 (14)	4 (7)	6 (14.5)	9 (21.5)	18 (15)
Absent	31 (12)	—	—	—	31 (25.5)
Total	68 (26)	4 (7)	6 (14.5)	9 (21.5)	49 (40.5)
Total decrease a–d	77 (29)	11 (19)	11 (27.5)	18 (43)	37 (30.5)
Decrease a–e	106 (40)	13 (22.5)	12 (30)	19 (45)	63 (52)
f. Satisfaction decreased	33 (12.5)	3 (5)	3 (7.5)	6 (14.5)	15 (12)
g. Sexual activity					
Decreased	62 (23.5)	6 (10)	9 (22)	15 (36)	32 (26)
Increased	27 (10.5)	11 (19)	2 (5)	2 (5)	12 (10)
Total change	89 (34)	17 (29)	11 (27)	17 (41)	44 (36)
h. Value of sexuality					
Decreased	19 (7)	2 (3.5)	3 (7.5)	4 (10)	11 (9)
Increased	39 (15)	11 (19)	4 (10)	5 (12)	19 (15.5)
Total change	58 (22)	13 (22.5)	7 (17.5)	9 (22)	30 (24.5)

W&S: intensive regular outpatient check-ups (Wait & See); RT: radiotherapy; PCT: polychemotherapy; RRRTM: resection of residual retroperitoneal tumor mass.

and PCT+RRRTM: 3.5%). Due to the low incidence of these problems, they were not analyzed any further. A decrease or absence of ejaculation was reported by 68 patients (26%); complete absence was mentioned exclusively by patients treated by PCT+RRRTM. A total of 77 patients reported a reduction of ≥1 aspects (a–d) of the sexual response (29%) (ejaculation included 106 patients [40%] reporting reduction of ≥1 functions). Thirty-three patients (12.5%) were dissatisfied about their sexual life since treatment. This mainly concerned patients who reported reduction of ≥2 sexual functions (16 patients, 49% of this group). 34% of the patients reported a change in sexual activity (n = 89; decrease: 23.5%, increase: 10.5%). Changes in the value of sexuality were reported by 22% (n = 58: decrease: 7.5%, increase: 15%). In addition to outcomes of the total population, Table 2 also provides an overview of the outcomes per treatment modality.

Comparison of the Various Treatment Groups

Table 3a presents the results of a comparison between the W&S group versus the other treatment modalities (RT, PCT, and PCT+RRRTM). Due to the fairly wide variation in mean age between the various treatment groups, not only the Mann-Whitney *U* test was used, but also ANOVA corrected for age. In Table 3b the standardized mean scores of the various treatment modalities are presented.

The scores in the group treated by RT were generally higher than those of the W&S group, but only the scores for sexual activity were significantly different. In the group treated by PCT, the scores were considerably higher than those in the W&S group; significant differences were found for almost all variables using the nonparametric tests, but application of ANOVA corrected for age showed significant differences only for decreased libido, orgasm, ejaculation, and for the index of the cumulative scores and changes in sexual activity. The scores in the group treated by PCT+RRRTM were generally much higher than those in the W&S group; it was surprising that on all points the scores in this group were lower than those in the PCT group. After correction for age, differences between this group and the W&S group were significant for ejaculation, the index of the cumulative scores, sexual dissatisfaction, and changes in sexual activity. In addition, ejaculation in this group differed significantly from that in the RT and PCT groups (vs. RT: $P = 0.000$; vs. PCT: $P = 0.002$; data not shown).

Correlation between Dependent Variables and Covariables

The correlation between the scores for the sexual response functions (libido, arousal, erection, and orgasm) was fairly high and these variables form a homogeneous scale (Spearman's Rho: 0.55–0.74; Cronbach's α: 0.89), whereas the correlation between these

TABLE 3a
Differences in Sexual Functioning Depending on Treatment: "Wait & See" (n = 59) versus RT (n = 41), PCT (n = 42), and PCT + RRRTM (n = 122)

PCT + RRRTM[a]	W & S vs. RT[a]	Corr. age[b]	W & S vs. PCT[a]	Corr. age[b]	W & S vs. PCT + RRRTM[a]	Corr. age[b]
a. Libido	NS[c]	NS	0.019	0.033	0.036	NS
b. Arousal	NS	NS	0.035	NS	0.042	NS
c. Erection	NS	NS	0.056	NS	NS	NS
d. Orgasm	NS	NS	0.010	0.014	NS	NS
e. Ejaculate	NS	NS	0.031	0.04	0.000	0.000
Index a-d	NS	NS	0.006	0.017	0.012	0.047
Index a–e	NS	NS	0.004	0.004	0.000	0.001
f. Satisfaction	NS	NS	0.041	NS	0.020	0.041
g. Sexual activity	0.016	NS	0.001	0.005	0.006	0.023
h. Value of sexuality	NS	NS	NS	NS	NS	NS

W&S: intensive regular outpatient check-ups (Wait & See); RT: radiotherapy; Corr.: corrected for age; PCT: polychemotherapy; RRRTM: resection of residual retroperitoneal tumor mass; NS: not significant.
[a] Determined using the Mann–Whitney *u* test.
[b] Analysis of variance corrected for age.
[c] All nonsignificant values were $P > 0.05$.

TABLE 3b
Means of the Raw Scores (Standardized into a Scale 0–10) for Sexual Functioning per Treatment group (n = 264)

	Total mean (SD)	W & S	RT	PCT	PCT + RRRTM
a. Libido	−2.31 (2.95)	−1.47	−2.44	−3.02	−2.43
b. Arousal	−1.59 (2.58)	−0.90	−1.71	−1.98	−1.75
c. Erection	−1.45 (2.82)	−0.73	−1.67	−1.87	−1.58
d. Orgasm	−2.17 (3.22)	−1.44	−1.54	−3.17	−2.38
e. Ejaculate	−2.17 (3.69)	−0.45	−0.98	−1.43	−3.55
Index a-d	−1.90 (2.53)	−1.15	−1.88	−2.56	−2.04
Index a-e	−1.95 (2.39)	−1.01	−1.67	−2.34	−2.35
f. Satisfaction	−1.78 (2.85)	−1.07	−1.38	−2.14	−2.13
g. Sexual activity	−0.24 (1.30)	+0.26	−0.33	−0.60	−0.33
h. Value of sexuality	+0.18 (1.17)	+0.38	+0.06	+0.06	+0.17

SD: standard deviation; W & S: intensive regular outpatient check-ups (Wait & See); RT: radiotherapy; PCT: polychemotherapy; RRRTM: resection of residual retroperitoneal tumor mass; +: increase; −: decrease.

variables and ejaculation, and the item-total correlation of ejaculation was rather low and decreased the Cronbach's α (Spearman's Rho: 0.22–0.33; item-total correlation: 0.37; Cronbach's α: 0.84). Sexual satisfaction showed a reasonably strong correlation with the scores for the sexual response functions: libido, arousal, erection, and orgasm (Spearman's Rho: 0.56–0.62), but the correlation with decreased ejaculation was less strong (Spearman's Rho: 0.43). Changes in sexual activity showed a moderate correlation with the sexual response functions (libido, arousal, erection, and orgasm) (Spearman's Rho: 0.40–0.48) and a low correlation with ejaculation (Spearman's Rho: 0.20). The correlation with changes in the value of sexuality was not significant or very low (Spearman's Rho: 0.12–0.23) (Table 4a). Although there were significant differences in age and follow-up period between the four treatment groups (Table 1), these variables, as well as the stage of the disease and the presence of other complaints or diseases, showed only weak correlations with the scores for reduced sexual functioning (Spearman's Rho: < 0.12–0.31) (Table 4b).

DISCUSSION

This large-scale study on 337 patients (total response: n = 287, 85%; included patients: n = 264, 78%) provides information about changes in sexual functioning after treatment for testicular cancer as perceived by

TABLE 4a
Correlation between Sexual Variables (Spearman's Rho $P < 0.05$) (n = 264)

	Li	Ar	Er	Or	Ej	Sa	Act	Value
a. Libido	1.00							
b. Arousal	0.74	1.00						
c. Erection	0.55	0.71	1.00					
d. Orgasm	0.58	0.65	0.67	1.00				
e. Ejaculate	0.29	0.22	0.33	0.32	1.00			
f. Satisfaction	0.56	0.56	0.58	0.62	0.43	1.00		
g. Sexual activity	0.48	0.48	0.40	0.41	0.20	0.41		
h. Value	0.23	0.20	NS[a]	NS	NS	0.24	NS	
Index a–d	0.87	0.83	0.75	0.84	0.34	0.66	−0.48	NS
Index a–e	0.81	0.76	0.72	0.79	0.61	0.69	−0.46	NS

Li: libido; Ar: arousal; Er: erection; Or: orgasm; Ej: ejaculate; Sa: satisfaction; Act: sexual activity; NS: not significant.
[a] All nonsignificant avlues were Spearman's Rho $P < 0.12$.

TABLE 4b
Correlation between Sexual Variables and Covariables (Spearman's Rho $P < 0.05$) (n = 264)

	Age	Follow-up	Stage	Other diseases
a. Libido	0.19	NS[a]	0.14	0.21
b. Arousal	0.27	0.16	0.12	0.16
c. Erection	0.30	0.14	NS	0.21
d. Orgasm	0.15	0.12	0.16	NS
e. Ejaculate	NS	0.21	0.31	0.18
f. Satisfaction	0.19	0.21	0.16	0.25
g. Sexual activity	0.26	NS	0.17	0.16
h. Value of sexuality	0.25	NS	NS	NS
Index a–d	0.23	0.13	0.18	0.20
Index a–e	0.27	0.20	0.26	0.22

[a] All nonsignificant values were Spearman's Rho $P < 0.12$.

the patients. It shows how the subjective appraisal of sexuality can be influenced by testicular cancer. Nearly 25% of the patients reported decreased sexual activity (23.5%), whereas >29% reported a decrease in ≥1 aspects of male sexual response (libido, arousal, erection, and orgasm). Decreased libido and orgasm were reported relatively more frequently than decreased arousal and erection. When ejaculation was included, 40% of respondents reported a decrease in ≥1 sexual functions. There was a moderate correlation between sexual dissatisfaction and a decrease in sexual response functions. Approximately 50% of the patients who reported a decrease in ≥2 sexual functions were dissatisfied. Compared with the situation prior to diagnosis and treatment, nearly 25% of patients stated that the value of their sexuality had changed.

Comparison of treatment modalities introduced important nuancing to the results of the total group, and only partly supported conclusions of previous research on physiologic aspects,[27] as well as conclusions of earlier studies comparing treatments.[14–15,18–20,22–23] In absolute terms, the W&S patients reported the least decrease in sexual functions and sexual activity. Although comorbidity does not apply to the W&S group, 22.5% of these patients nevertheless reported a decrease of ≥1 sexual functions. These findings appear to be somewhat different from those derived from research in healthy respondents, although no exact figures are available regarding disturbances in sexual functioning for the normal population. [66,67] It is difficult to explain this result on the basis of biologic-organic disturbances, because orchidectomy was the only medical interference. Emotional or cognitive factors, such as anxiety, impairment of physical integrity, feelings of loss, aversions, and loss of control, may play an important role.[6,14,17,20–22] The fact that approximately 25% of patients with Stage I disease treated with surveillance can be expected to recur and require chemotherapy[59] may also generate anxiety and stress. For this reason, it has been argued that patients should be offered the option of initial nerve-sparing retroperitoneal lymph node dissection (RPLND) versus surveillance.[68,69] However, it appears that doctors tend to overestimate the psychologic morbidity and underestimate the experienced physical complaints of testicular cancer patients, in particular patients treated by W&S,[70] although the eventual psychosomatic component of these complaints remains unclear.

The RT group was an average of 9 years older that the W&S group, but the 2 groups did not differ significantly in any aspect except decreased sexual activity. Correlations between sexual functioning and age were generally weak and correction of the scores for age did not change the general trend. Erectile dys-

function due to RT-induced vascular damage appears unlikely because only a few RT patients reported erectile problems (14.5%). A large proportion of the RT group mentioned decreased libido and sexual activity (22% each). It is unlikely that these problems were caused by low testosterone levels because generally measurements of serum testosterone are within the normal ranges,[42] and even very low serum testosterone levels permit normal sexual functioning.[32,33] In this respect, emotional and cognitive factors also may be decisive.

In the group treated by PCT (±RRRTM) a limited number of patients reported erectile problems (17% and 15%, respectively), and there was no statistic significant difference compared with the W&S group. Therefore, PCT-induced erectile dysfunction could not be proven. However, a considerable proportion of PCT patients reported decreased libido (29.5%) and orgasm (28.5%). In addition, after correction for age, this group still differed significantly from the W&S group. Theoretically, these differences may have been caused by long term biologic impacts of PCT such as neuropathy and general health status, but at the same time interaction with emotional and cognitive factors may have played a decisive role in view of the life-threatening nature of cancer in general and the drastic nature of PCT.[15,16,23] The same applies to the decrease in sexual activity, as was reported by nearly 25% of the patients. For a patient undergoing a course of PCT, the situation is more or less impossible to control because of the paradoxic nature of this aggressive treatment, and the patient's unclear future. Such massive loss of control can give rise to passivity[71] and perhaps even to emotional regression.[72]

According to expectations,[73–75] the sharpest decrease in ejaculation was reported in the PCT+RRRTM group. This group was the only one that reported absence of ejaculation, e.g., retrograde ejaculation. However, contrary to expectations, considerably less decrease in libido, orgasm, and sexual activity was reported (although the differences were not statistically significant) in the group treated by PCT+RRRTM than in the group treated by PCT alone. This trend underscores the lack of evidence for a mere biologic-organic-based decrease in sexual functioning after treatment by PCT. From a psychologic point of view, chemotherapy may give rise to uncertainty, anxiety, and passivity, whereas additional resection of residual tumor mass after chemotherapy (PCT + RRRTM) may increase feelings of recovery and certainty by its concrete effect. This same argument has been stated with respect to the discussion concerning nerve-sparing RPLND versus surveillance in Stage I NSGCT.[70]

In general, uncertainty, anxiety, and loss of control appear to have an inhibitory influence on sexual functioning,[76,77] although this relation also may occur in reverse.[78] In addition, negative fixation on the genital region can lead to a decrease in sexual activity.[79] As in patients with gynecologic cancers,[80] changes in the experience of sexuality and sexual behavior in patients treated for testicular cancer can only partly be explained by biologic-organic disturbances. Although patients receiving PCT are at risk for sexual morbidity, changes in sexual functioning appear to be strongly related to emotional, cognitive, and motivational aspects.[11,56,81,82] In this respect, it was noteworthy that a decrease in one or more sexual functions led to reduced sexual satisfaction in only a limited number of patients.[14] It is possible that after a cancer diagnosis, which carries a heavy emotional burden and involves a life-threatening experience, patients rebalance their emotions and cognitions, such as norms and values concerning sexuality and the partner relationship.[15,18,21] This may give rise to shifts in their outlook.[83,84]

CONCLUSIONS

A substantial proportion of the patients treated for testicular cancer in the current study experienced a decrease in sexual functioning, although the majority reported no symptoms at all. Comparisons between treatment groups introduced important nuancing to the results and showed significant differences between patient groups. Patients treated by PCT (±RRRTM) reported a considerably sharper decrease in sexual functions, satisfaction, and activity than the W&S group. Therefore, chemotherapy can be considered to be the main risk factor for a decrease in sexual functioning.

The differences between treatment groups in reduction of sexual functions could not be attributed to age, the duration of follow-up, tumor stage, or the presence of other diseases, because these variables showed only very weak correlations with the variables concerning sexuality. Furthermore, there were no differences in demographic variables or reports of other abnormalities between the treatment groups. Theoretically, treatment-related biologic-organic factors, such as hormonal, vascular, or neurogenic disturbances, may be held responsible for reduced sexual functioning, but this has yet to be demonstrated. Psychologic factors appear to play an important mediating (if not determining) role. If future studies confirm this theory, psychologic intervention would be of benefit for patients with decreased sexual functioning after treatment for testicular cancer.

REFERENCES

1. Adami HO, Bergstrom R, Mohner M, Zatonski W, Storm H, Ekbom A, et al. Testicular cancer in nine northern European countries. *Int J Cancer* 1994;59:33–8.
2. Mostofi FK. Testicular tumors: epidemiologic, etiologic, and pathologic features. *Cancer* 1973;32:1186–201.
3. Visser O, Coebergh JWW, Schouten LJ, editors. Incidence of cancer in the Netherlands, 1993. Utrecht: The Netherlands Cancer Registry, 1996.
4. Fossa SD, Aass N, Kaalhus O. Testicular cancer in young Norwegians. *J Surg Oncol* 1988;39:43–63.
5. Weijmar Schultz WCM, Wiel van de HBM, Bouma J, Janssens J, Littlewood J. Psychosexual functioning after the treatment of cancer of the vulva. A longitudinal study. *Cancer* 1990;66: 402–7.
6. Auchincloss SS. Sexual dysfunction in cancer patients: issues in evaluation and treatment. In: Holland JC, Rowland JH, editors. Handbook of psycho-oncology, the psychological care of the patient with cancer. New York: Oxford University Press, 1989:383–413.
7. Auchincloss SS. Sexual dysfunction after cancer treatment. *J Psychosoc Oncol* 1991;9:23–42.
8. Schover LR, Jensen SB. Sexual problems and chronic disease: a comprehensive approach. New York: Guilford Press, 1988.
9. Weijmar Schultz WCM, van de Wiel HBM. Sexual functioning after gynaecological cancer treatment. Groningen: Dijkhuizen Van Zanten B.V., 1991.
10. Andersen BL. Sexual functioning morbidity among cancer survivors. *Cancer* 1985;55:1835–42.
11. Bancroft J, Wu FCW. Changes in erectile responsiveness during androgen therapy. *Arch Sex Behav* 1983;12:59–66.
12. Masters WH, Johnson VE. Human sexual response. Boston: Little, Brown, 1966.
13. Kaplan HS. Disorders of sexual desire. New York: Brunner/ Mazel, 1979.
14. Aass N, Grunfeld B, Kaalhus O, Fossa SD. Pre- and post-treatment sexual life in testicular cancer patients: a descriptive investigation. *Br J Cancer* 1993;67:1113–7.
15. Gritz E, Wellisch D, Wang HJ, Siau J, Landsverk JA, Cosgrove MD. Long-term effects of testicular cancer on sexual functioning in married couples. *Cancer* 1989;64:1560–7.
16. Stoter G, Koopman A, Vendrik CP, Struyvenberg A, Sleijfer DTh, Willemse PHB, et al. Ten-year survival and late sequelae in testicular cancer patients treated with cisplatin, vinblastine, and bleomycin. *J Clin Oncol* 1989;7:1099–104.
17. Moynihan C. Testicular cancer: the psychosocial problems of patients and their relatives. *Cancer Surv* 1987;6:477–510.
18. Schover LR, von Eschenbach AC. Sexual and marital relationships after treatment for nonseminomatous testicular cancer. *Urology* 1985;25:251–5.
19. Schover LR, Gonzalez M, von Eschenbach AC. Sexual and marital relationships after radiotherapy for seminoma. *Urology* 1986;27:117–23.
20. Tinkler SD, Howard GC, Kerr GR. Sexual morbidity following radiotherapy for germ cell tumours of the testis. *Radiother Oncol* 1992;25:207–12.
21. Rieker PP, Edbril SD, Garnick MB. Curative testis cancer therapy: psychosocial sequelae. *J Clin Oncol* 1985;3:1117–26.
22. Rieker PP, Fitzgerald EM, Kalish LA, Richie JP, Lederman GS, Edbril SD, et al. Psychosocial factors, curative therapies, and behavioral outcomes. A comparison of testis cancer survivors and a control group of healthy men. *Cancer* 1989; 64:2399–407.
23. Bloom JR, Fobair P, Gritz E, Wellisch DK, Spiegel D, Varghese A, et al. Psychosocial outcomes of cancer: a comparative analysis of Hodgkin's disease and testicular cancer. *J Clin Oncol* 1993;11:979–88.
24. Nijman JM, Schraffordt Koops H, Oldhoff J, Kremer J, Sleijfer DT. Sexual function after surgery and combination chemotherapy in men with disseminated nonseminomatous testicular cancer. *J Surg Oncol* 1988;38:182–6.
25. Kaasa S, Aass N, Mastekaasa A, Lund E, Fossa SD. Psychosocial well-being in testicular cancer patients. *Eur J Cancer* 1991;27:1091–5.
26. Blackmore C. The impact of orchidectomy upon the sexuality of the man with testicular cancer. *Cancer Nurs* 1988;11: 33–40.
27. van Basten JP, Jonker-Pool G, van Driel MF, Sleijfer DTh, van de Wiel HBM, Hoekstra HJ. The sexual sequelae of testicular cancer. *Cancer Treat Rev* 1995;21:479–95.
28. Willemse PH, Sleijfer DTh, Sluiter WJ, Schraffordt Koops H, Doorenbos H. Altered Leydig cell function in patients with testicular cancer: evidence for bilateral testicular defect. *Acta Endocrinol* 1983;102:616–24.
29. Nijman JM, Schraffordt Koops H, Kremer J, Willemse PH, Sleijfer DT, Oldhoff J. Fertility and hormonal function in patients with a nonseminomatous tumor of the testis. *Arch Androl* 1985;14:239–46.
30. Hansen PV, Trykker H, Andersen J, Helkjaer PE. Germ cell function and hormonal status in patients with testicular cancer. *Cancer* 1989;64:956–61.
31. Berthelsen JG, Engelholm SA, von der Maase H, Rorth M. Serum testosterone, LH, and FSH in patients with testicular cancer before and after radio- and chemotherapy. *Scand J Urol Nephrol* 1983;17:287–90.
32. Buena F, Swerdloff RS, Steiner BS, Lutchmansingh P, Peterson MA, Randian MR, et al. Sexual function does not change when serum testosterone levels are pharmacologically varied within the normal male range. *Fertil Steril* 1993;59:1118–23.
33. Gooren LJ. Androgen levels and sex functions in testosterone-treated hypogonadal men. *Arch Sex Behav* 1987;16:463–73.
34. Greenstein A, Plymate SR, Katz PG. Visually stimulated erection in castrated men. *J Urol* 1995;153:650–2.
35. Heim N. Sexual behavior of castrated sex offenders. *Arch Sex Behav* 1981;10:11–9.
36. Carani C, Bancroft J, Granata A, Del Rio G, Marrama P. Testosterone and erectile function, nocturnal penile tumescence and rigidity, and erectile response to visual erotic stimuli in hypogonadal and eugonadal men. *Psychoneuroendocrinology* 1992;17:647–54.
37. Bancroft J. Hormones and human sexual behavior. *J Sex Marital Ther* 1984;10:2–21.
38. von Eschenbach AC. Sexual dysfunction following therapy for cancer of the prostate, testis and penis. *Front Radiat Ther Oncol* 1980;14:42–50.
39. Ogilvy-Stuart AL, Shalet SM. Effect of radiation on the human reproductive system. *Environ Health Perspect* 1993; 101(Suppl 2):109–16.
40. Fossa SD, Klepp O, Aakvaag A. Serum hormone levels in patients with malignant testicular germ cell tumours without clinical and/or radiological signs of tumour. *Br J Urol* 1980;52:151–7.

41. Tomiç R, Bergman B, Damber JE, Littbrand B, Löfroth PO. Effects of external radiation therapy for cancer of the prostate on the serum concentrations of testosterone, follicle-stimulating hormone, luteinizing hormone and prolactine. *J Urol* 1983;130:287–9.
42. Fossa SD, Abyholm T, Norman N, Jetne V. Post-treatment fertility in patients with testicular cancer. III. Influence of radiotherapy in seminoma patients. *Br J Urol* 1986;58:315–9.
43. Swanson DA. Cancer of the bladder and prostate: the impact of therapy of therapy on sexual function. In: Von Eschenbach AC, Roderiquez DB, editors. Sexual rehabilitation of the urologic cancer patient. Boston: G.K. Hall & Co. 1981:89–107.
44. Goldstein I, Feldman MI, Deckers PJ, Babaian RK, Krane RJ. Radiation-associated impotence. A clinical study of its mechanism. *JAMA* 1984;251:903–10.
45. Bergman B, Damber JE, Litterand B, Sjögren K, Tomiç R. Sexual function in prostatic cancer patients treated with radiotherapy, orchiectomy or oestrogens. *Br J Urol* 1984;56:64–9.
46. El-Beheiry A, Souka A, El-Kamshoushi A, Hussein S, El-Sabah K. Hyperprolactinemia and impotence. *Arch Androl* 1988;21:211–4.
47. Aass N, Fossa SD, Theodorsen L, Norman N. Prediction of long-term gonadal toxicity after standard treatment for testicular cancer. *Eur J Cancer* 1991;27:1087–91.
48. Vogelzang NJ, Bosl GJ, Johnson K, Kennedy BJ. Raynaud's phenomenon: a common toxicity after combination chemotherapy for testicular cancer. *Ann Intern Med* 1981;95:288–92.
49. Roth BJ, Greist A, Kubilis PS, Williams SD, Einhorn LH. Cisplatin-based combination chemotherapy for disseminated germ cell tumors: long-term follow-up. *J Clin Oncol* 1988;6:1239–47.
50. van Driel MF, van der Wiel HBM, Mensink HJA. Some mythologic, religious, and cultural aspects of impotence before the present modern era. *Int J Impot Res* 1994;6:163–9.
51. Wood DP, Herr HW, Heller G, Vlamis V, Sogani PC, Motzer RJ, et al. Distribution of retroperitoneal metastases after chemotherapy in patients with nonseminomatous germ cell tumours. *J Urol* 1992;148:1812–5.
52. Tekgul S, Ozen HA, Celebi I, Ozgu I, Ergen A, Demircin B, et al. Postchemotherapeutic surgery for metastatic germ cell tumours: results of extended primary chemotherapy and limited surgery. *Urology* 1994;43:349–54.
53. Aprikian AG, Herr HW, Bajorin DF, Bosl GJ. Resection of postchemotherapy residual masses and limited retroperitoneal lymphadenectomy in patients with metastatic testicular nonseminomatous germ cell tumors. *Cancer* 1994;74:1329–34.
54. Jones DR, Norman AR, Horwich A, Hendry WF. Ejaculatory dysfunction after retroperitoneal lymphadenectomy. *Eur Urol* 1993;23:169–71.
55. Sheinfield J, Bajorin D. Management of the postchemotherapy residual mass. *Urol Clin North Am* 1993;20:133–43.
56. Rosen RC, Beck JG. Patterns of sexual arousal. New York: Guildford Press, 1988.
57. Nijman JM, Jager S, Boer PW, Kremer J, Oldhoff J, Schraffordt Koops H. The treatment of ejaculation disorders after retroperitoneal lymph node dissection. *Cancer* 1982;50:2967–71.
58. Peckham MJ, Barret A, Horwich A, Hendry WF. Orchiectomy alone for stage I testicular nonseminoma. A progress report on the Royal Marsden Hospital Study. *Br J Urol* 1983;55:754–9.
59. Gels ME, Hoekstra HJ, Sleijfer DT, Marrink J, de Bruijn HWA, Molenaar WM, et al. Detection of recurrence in patients with clinical stage I nonseminomatous testicular germ cell tumors and consequences for further follow-up: a single-center 10-year experience. *J Clin Oncol* 1995;13:1188–94.
60. Einhorn LH. Treatment of testicular cancer: a new and improved model. *J Clin Oncol* 1990;8:1777–81.
61. Stoter G, Sleijfer DT, Vendrik CP, Schraffordt Koops H, Struyvenberg A, van Oosterom AT, et al. Combination chemotherapy with cis-diammine-dichloro-platinum, vinblastine, and bleomycin in advanced testicular non-seminoma. *Lancet* 1979;1:941–5.
62. Gelderman WA, Schraffordt Koops H, Sleijfer DT, Oosterhuis JW, van der Heide JN, Mulder NH, et al. Results of adjuvant surgery in patients with stage III and IV non-seminomatous testicular tumors after cisplatin-vinblastine-bleomycin chemotherapy. *J Surg Oncol* 1988;38:227–32.
63. Donohue JP, Thornhill JA, Foster RS, Bihrle R, Rowland RG, Einhorn LH. The role of retroperitoneal lymphadenectomy in clinical stage B testis cancer: the Indiana University experience (1965 to 1989). *J Urol* 1995;153:85–9.
64. Horwich A, Dearnaley DP. Treatment of seminomas. *Semin Oncol* 1992;19:171–80.
65. Marks LB, Anscher MS, Shipley WK. The role of radiation therapy in the treatment of testicular germ cell tumors. *Hematol Oncol Clin North Am* 1991;5:1143–72.
66. Spector IP, Carey MP. Incidence and prevalence of the sexual dysfunctions: a critical review of the empirical literature. *Arch Sex Behav* 1990;19:389–408.
67. Frenken J. Sexual dysfunctions in the Netherlands (in Dutch). *MGV* 1987;1:3–18.
68. Foster RS, Donohue JP. Surgical treatment of clinical stage A nonseminomatous testis cancer. *Semin Oncol* 1992;19:166–70.
69. Donohue JP, Thornhill JA, Foster RS, Rowland RG, Bihrle R. Retroperitoneal lymphadenectomy for clinical stage A testis cancer (1965 to 1989): modifications of technique and impact on ejaculation. *J Urol* 1993;149:237–43.
70. Fossa SD, Moynihan C, Serbouti S. Patients' and doctors' perception of long-term morbidity in patients with testicular cancer clinical stage I. A descriptive pilot study. *Support Cancer Care* 1996;4:118–28.
71. Cella DF, Tross S. Psychological adjustment to survival from Hodgkin's disease. *J Consult Clin Psychol* 1986;54:616–22.
72. Corradi RB. Psychological regression with illness. *Psychosomatics* 1983;24:353–8.
73. Nijman JM, Schraffordt Koops H, Oldhoff J, Kremer J, Jager S. Sexual function after bilateral retroperitoneal lymph node dissection for nonseminomatous testicular cancer. *Arch Androl* 1987;18:255–67.
74. Narayan P, Lange PH, Fraley EE. Ejaculation and fertility after extended retroperitoneal lymph node dissection for testicular cancer. *J Urol* 1982;127:685–8.
75. Richie JP. Clinical stage I testicular cancer: the role of modified retroperitoneal lymphadenectomy. *J Urol* 1990;144:1160–3.
76. Barlow DH. Causes of sexual dysfunction: the role of anxiety and cognitive interference. *J Consult Clin Psychol* 1986;54:140–8.

77. Dekker J, Everaerd W. A study suggesting two kinds of information processing of the sexual response. *Arch Sex Behav* 1989;18:435–47.
78. Rowland DL, Cooper SE, Houtsmuller EE. Sexual functioning and emotional response of men (in Dutch). *Tydschrift voor Seksuologie* 1996;20:303–15.
79. Faith MS, Schare ML. The role of body image in sexually avoidant behavior. *Arch Sex Behav* 1993;22:345–56.
80. Weijmar Schultz WCM, Bransfield DD, van de Wiel HBM, Bouma J. Sexual outcome following female genital cancer treatment, a critical review of methods of investigation and results. *Sex Marital Ther* 1992;7:29–64.
81. Fryda NH. The sexual emotions (in Dutch). *De Psycholoog* 1993;28:278–84.
82. Haas K, Haas A. Understanding sexuality. St. Louis: C. V. Mosby, 1993.
83. Quigley KM. The adult cancer survivor: psychosocial consequences of cure. *Semin Oncol Nurs* 1989;5:63–9
84. Lazarus RS. Cognition and motivation in emotion. *Am Psychol* 1991;46:352–67.