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Surviving testicular cancer

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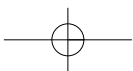
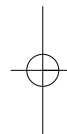
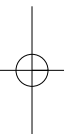
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**chapter 5 testicular cancer:
a longitudinal pilot study on
stress response symptoms and
quality of life in couples before
and after chemotherapy**

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Introduction

Testicular cancer is a rare disease, although it is the most common tumour in men aged 20-35 years. About 500 new cases are diagnosed each year in the Netherlands (1). Testicular cancer is distinguished into seminomas and non-seminomas, and each type accounts for about half of the total. Half of the men with a non-seminoma are diagnosed with disseminated disease, that is treated with chemotherapy (2). Since the introduction of cisplatin-based chemotherapy in the late nineteen seventies, up to 80% of the patients with disseminated disease can be cured (3-5).

Chemotherapy for testicular cancer has several acute physical side effects like nausea, fatigue, and neuropathy (6). On a psychological level, patients receiving chemotherapy have been found to report anxiety, depression and distress (7-10). The partners of testicular cancer patients receiving chemotherapy may encounter adverse sequelae, as well. Partners have to struggle with the fear of potentially losing their significant other. Partners are the primary source of information for family members and friends, while their husbands are admitted to the hospital. In addition to this social task, partners often take on the caregiver role between chemotherapy cycles. Care giving for cancer patients has been found to negatively impact on caregiver's physical and mental health (11-13).

The impact of testicular cancer on younger couples might differ from the impact on couples who face cancer at an older age. The young couples confronted with testicular cancer might not have been together for a substantial period of time. This can make the relationship more vulnerable to the stressors induced by major life events. Earlier studies have showed that relationships of shorter duration are more sensitive to disruption after a testicular cancer diagnosis (14;15), although another study did not find such a connection (16). Also, couples are confronted with possible treatment-related infertility and sexual difficulties at a time in life where partners are often focused on starting a family. Couples may face several individual and dyadic stressors after the diagnosis of testicular cancer, leading to the experience of distress and lowered quality of life. This is particularly true when chemotherapy is part of the treatment protocol, as it is a more demanding treatment modality than surgery alone, in the case of testicular cancer.

Several prospective studies focused on dyadic adjustment and functioning from cancer diagnosis in a variety of sites, up to one and a half year later (17-20). Although both patients and partners were reported to suffer from distress, levels of distress did not necessarily correspond within couples. Different patterns of distress and adjustment were found to be associated with gender and health status. Some studies reported that female partners were most vulnerable since they reported higher levels of distress than female and male patients and male partners (20-22).

One pilot study examined the course of distress and quality of life in testicular cancer patients before, during and after chemotherapy (complete data on 10 patients) (23). Patients reported highest levels of distress shortly before the start of chemotherapy. Distress

and anxiety decreased over time. We chose to expand the findings of this study by including partners in our study in order to investigate the adjustment of couples facing testicular cancer during the first year after diagnosis. Patterns of stress response symptoms and quality of life of patients and partners were examined at three time points during the first year. Goals of the present study were: (1) to explore differences and relationships between patients' and partners' stress response symptoms and quality of life (QoL); (2) to examine change over time in stress response symptoms and QoL in patients and partners; (3) to relate earlier levels of stress response symptoms and QoL in patients and partners to later levels; and (4) to examine differences in QoL of patients and partners with that of a reference group of men and women.

Methods

Procedure and participants

All patients diagnosed with a disseminated nonseminomatous testicular tumour, who consecutively visited the University Medical Center Groningen (UMCG) in The Netherlands for treatment between April 2001 and March 2004, and who were married or cohabiting were approached for this study. Exclusion criteria were a psychiatric history, age younger than 18 years at study entry, insufficient command of the Dutch language, and previous treatment for cancer. The study was introduced to the patients and their partners after orchiectomy (removal of the affected testicle) was performed. Couples received a questionnaire at the following three time points: after orchiectomy but before the start of chemotherapy (T1), immediately after chemotherapy completion, which is approximately three months after T1 (T2), and one year after T1 (T3). The patients received four cycles of cisplatin, etoposide and bleomycin, with a three-week interval between each cycle. Couples received a letter with information about the objectives of the study, an informed consent form, the questionnaires, and a prepaid return envelope. Thirty eligible couples were approached to participate in the study, of whom 21 participated (70%). Two couples did not complete all three measurement times, therefore 19 couples provided complete data. The study was approved by the Medical Ethics Committee of the University Medical Center Groningen.

Measurements

Sociodemographics: Data on the following sociodemographic variables were collected at T1: age, educational level, employment status, and duration of the relationship. Highest educational level completed was measured on a seven-point scale: primary school [1], and lower vocational [2], lower secondary [3], middle secondary [4], high secondary [5], higher vocational degrees [6], and university [7]. Employment status could be indicated as employed for wages, housekeeping, student, unemployed, unable to work, or retired.

Stress response symptoms were measured with the Impact of Event Scale (24;25). This scale (15 items) makes an inventory of the extent to which a subject is currently occupied with an

event by measuring intrusion (intrusively experienced ideas, images, feelings or bad dreams about the event, 7 items) and avoidance of unpleasant feelings or memories of the event (8 items). The IES is often used in studies on cancer patients (26). With this questionnaire, information was obtained about the degree to which confrontation with testicular cancer was influencing the current daily life of the respondent. Higher scores indicate more stress response symptoms. A total score of more than 26 indicates severe stress response symptoms, for which psychological help is recommended. Reliability of this scale was good for patients (Cronbach's alpha for the different measurement times ranged from 0.82 to 0.89) and for partners (Cronbach's alpha for the different measurement times ranged from 0.78 to 0.93).

Quality of life was measured with three subscales of the RAND-36 (27): physical functioning (10 items), social functioning (2 items) and mental health (5 items). To avoid statistical problems due to multiple comparisons, we chose these three subscales as a representation of overall QoL. The RAND-36 measures generic QoL. After recoding and transformation, scores on the subscales could range from 0 to 100. Higher scores indicate a better QoL. Reliability of these scales was good to very good for patients (Cronbach's alpha for the different measurement times ranged from 0.67 to 0.90) and for partners (Cronbach's alpha for the different measurement times ranged from 0.75 to 0.92). The Dutch manual for the RAND-36 provides reference scores. These comprised the mean scores of a group of 691 non-selected men and 372 non-selected women from a random representative sample of persons aged 18 years and older from the population register of a municipality in the north of The Netherlands (no. of inhabitants = 108,000). The mean age of the persons in the total random sample was 44.1 years (range 18-89 years) (27).

Statistical analyses

Paired *t*-tests and Chi-square test were performed to examine differences in sociodemographics between patients and partners. Wilcoxon signed rank test (because of small sample size) and correlations were computed to examine differences and relationships in stress response symptoms and QoL between patients and partners. Repeated measures analysis of variance (ANOVA) was used to examine change over time in functioning. Pearson's product moment correlations were calculated to examine relationships between the functioning of patient and that of the partner and between measurement times. Strong correlation coefficients (>0.50) indicate consistency between measurement times and stable responses between earlier and later levels of functioning. Independent *t*-tests were performed to compare QoL of patients and partners with those of a reference group of men and women.

Results

Sociodemographic and treatment related variables

Sociodemographic and treatment related variables are reported in Table 1. Patients were older than partners ($t=-3.1$, $p<0.01$). Eighteen patients were employed for wages and one was a student, whereas eleven partners were employed for wages, four were home-keepers and the remaining four partners were students (Chi-square = 19.0, $p=0.04$). After chemotherapy was completed (at T2), all patients were restaged. Patients without biochemical or radiological abnormalities were considered to have reached complete remission ($n=8$). In case of proven residual disease, a resection of residual retroperitoneal tumour mass (RRRTM) was performed. Eleven patients underwent this surgery and were considered to be in complete remission afterwards. None of the 19 patients experienced a relapse during follow up (up to T3).

Table 1 Descriptives sociodemographic and treatment related variables

	Patient		Partner	
	Mean	SD	Mean	SD
Age (years) **	31.6	6.6	28.9	7.6
Range	19.9 – 43.5		19.8 – 44.7	
Duration relationship (years)	5.7	6.3		
Range	1 - 22			
Education level	3.6	1.4	4.0	1.6
	N	%	N	%
Employment status *				
Employed for wages	18	95%	11	58%
Student	1	5%	4	21%
Housewife			4	21%
RRRTM +				
Yes	11	58%		
No	8	42%		

* $p < 0.05$, ** $p < 0.01$

+ RRRTM resection of residual retroperitoneal tumour mass

Relationships between patients' stress response symptoms and QoL and those of partners

At T1, stress response symptoms of patients were moderately strongly and negatively related to those of partners ($r = -0.48$, $p < .05$). At T2, social functioning of patients was moderately strongly and positively related to that of partners ($r = 0.53$, $p < .05$). At the three measurement times all other correlations between patients' stress response symptoms and QoL and those of partners were low to moderate, ranging from $r = 0.04$ to $r = 0.34$, and not statistically significant. At T1, in two couples, both patient and partner experienced stress response symptoms above the cut-off point. At T2 and T3 there were no couples in which both patient and partner experienced stress response symptoms above the cut-off point. Wilcoxon tests showed only one significant difference between patients' and partners' functioning. At T2, patients reported a lower level of physical functioning than did partners ($Z = -2.6$, $p < 0.01$).

The course of stress response symptoms and QoL over time in patients and partners

Repeated measures ANOVA showed that the stress response symptoms of patients fluctuated according to a quadratic trend: the highest level was reported at T1, and after a decrease at T2, the level went up again somewhat at T3. Earlier levels of stress response symptoms in patients were highly positively related to later levels (Table 2). At T1, 5 of the patients (26%) reported stress response levels above the cut off point; at T2, 2 patients (11%); and at T3, 3 patients (16%). Two patients reported clinically elevated levels of stress response levels at all measurement times. For partners the level of stress response symptoms declined, via a linear trend. Partners' reports of stress response levels were moderately strongly related between T1 and T2, strongly between T2 and T3, and the relationship between T1 and T3 was weak (Table 2). At T1, 10 of the partners (53%) reported stress response levels above the cut off point, at T2, 6 (32%) and at T3, 2 (10.5%). One partner reported clinically elevated levels of stress response levels at all measurement times.

Lower physical functioning was reported by patients at T2 as compared to T1, but physical functioning returned to baseline level at T3. Earlier levels of physical functioning in patients were not significantly related to later levels, and correlations were low. A decline in social functioning of patients was also found at T2 compared to T1, but higher social functioning than at baseline was found at T3. Social functioning of patients at T1 was positively and strongly related to functioning at T2, but the relationships between T2 - T3 and T1 - T3 were low to moderate. Mental health of patients improved over time. Mental health at T1 was positively and strongly related to levels at T2, and weakly to levels at T3. The relationship between mental health at T2 and T3 was moderately strong.

For partners, no significant time effects were found for physical functioning and mental health. Earlier levels of physical functioning and mental health of partners were highly and positively related to later levels. Social functioning of partners improved over the year, and was highly positively related between T1 and T2, and between T1 and T3. The relationship between T2 and T3 was moderately strong. (Table 2).

Table 2 Stress response symptoms and Quality of Life of patients and partners

	T1	T2	T3	Reference group	Repeated measures ANOVA		T1 - T2	T2 - T3	T1 - T3	
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	F	p	r	p	r	p
Stress response symptoms										
Patient	18.1 (13.0)	10.2 (10.7)	12.3 (9.9)		7.9	.012	0.65	.002	0.71	.001
Partner	25.8 (9.3)	15.2 (12.6)	12.1 (12.4)		17.7	.001	0.41	<i>ns</i>	0.64	.003
										<i>ns</i>
Physical functioning										
Patient	93.4 (10.8)	70.5 (23.4)	92.6 (13.3)	84.5 (22.3) ^{oo##+}	21.4	.0001	0.28	<i>ns</i>	0.38	<i>ns</i>
Partner	90.2 (19.0)	90.8 (19.0)	89.7 (19.9)	80.7 (23.6) ^{o#}	0.19	<i>ns</i>	0.79	.0001	0.80	.0001
										0.20
Social functioning										
Patient	77.6 (19.7)	71.1 (22.8)	90.8 (13.1)	88.4 (19.6) ^{o##}	9.0	.008	0.61	.009	0.19	<i>ns</i>
Partner	72.1 (20.2)	77.6 (20.7) ^{**}	84.5 (16.5)	86.1 (20.9) ^{oo}	12.9	.002	0.60	.007	0.37	<i>ns</i>
										0.68
Mental health										
Patient	68.2 (22.3)	77.5 (11.9)	81.9 (13.4)	79.4 (17.3) ^o	6.7	.019	0.55	.017	0.33	<i>ns</i>
Partner	69.1 (13.6)	71.2 (15.6)	74.3 (15.1)	75.5 (18.9)	2.6	<i>ns</i>	0.72	.0001	0.64	.004
										0.52

Wilcoxon test patients and spouses ** p < 0.01
 independent t-test T1 and reference group ^o p < 0.05, ^{oo} p < 0.01
 independent t-test T2 and reference group [#] p < 0.05, ^{##} p < 0.01
 independent t-test T3 and reference group ⁺ p < 0.05

QoL of patients and partners compared to that of a reference group of men and women At T1, patients ($t=-3.4$, $p<0.01$) and partners ($t=-2.1$, $p<0.05$) reported better physical functioning than the reference groups. Patients ($t=2.3$, $p<0.05$) and partners ($t=2.9$, $p<0.01$) reported worse social functioning than the reference groups at T1, and patients ($t=2.2$, $p<0.05$) reported worse mental health at T1. At T2, patients reported worse physical functioning than the reference group of men ($t= 2.6$, $p<0.02$) but partners reported better physical functioning than the reference group of women ($t=-2.2$, $p<0.05$). Patients also reported worse social functioning than the reference men at T2 ($t=3.3$, $p<0.01$). No differences were found between the patients' and partners' mental health and the norm groups at T2. Only one significant difference was found at T3: patients reported better physical functioning than men in the reference group ($t = -2.6$, $p <0.02$) (Table 2).

Discussion

The present study was the first to prospectively and longitudinally examine psychosocial functioning in testicular cancer patients and their partners. We focused on stress response symptoms and quality of life (physical functioning, social functioning and mental health) after orchiectomy but before the start of chemotherapy, immediately after completion of chemotherapy, and nine months later (one year follow-up).

Stress response symptoms in couples were most salient before the start of chemotherapy. Twenty-six percent of patients reported clinically elevated stress response symptoms at this time, a number comparable to the 30% of patients with clinically elevated distress found in a recent study on testicular cancer patients (28). A review of stress response syndromes in adult cancer populations showed that the incidence of clinically elevated stress response symptoms ranged from 3% to 4% in patients recently diagnosed with early stage cancer (26). The majority of these studies used the same questionnaire for measuring stress response symptoms as we did. The same review identified younger age, greater proximity to diagnosis, more advanced disease and greater treatment intensity as risk factors for a higher level of stress response symptoms. The much higher percentage found in our study at the first measurement time may be explained by the prevalence of these four risk factors in our patient group. Not only did patients appear distressed, but also almost twice as many of the partners as compared to patients reported clinically elevated levels of stress response symptoms. Female sex has been found to correlate with greater stress response symptomatology in cancer populations (26). Of course, these spouses are not patients themselves, but obviously they face cancer related fears and worries as well. Our results affirm earlier findings that female spouses of cancer patients are vulnerable to distress, and often report higher levels of distress as compared to their male counterparts (20;21;29-31).

Stress response symptoms in couples decreased after completion of chemotherapy. One year after diagnosis, stress response levels in patients rose slightly, but they continued to decrease in partners. These patterns suggest that the period before chemotherapy commences is most

stressful, and that recovery seems to occur within a year. At the time of the first measurement the responses of the couples seem to be coloured by the fact that they had recently learned the diagnosis, and the outcome of treatment remained uncertain. Concerns of couples about side effects of chemotherapy such as nausea, the possibility of immunodeficiency and hair loss may contribute to distress. Partners also have caregiving tasks that can exacerbate their distress (22). All couples in this study received positive news about the results of treatment, and one year after diagnosis none of the patients had experienced a relapse of disease. Couples seemed to have recovered from this major life event over the year, possibly as a consequence of the success of treatment reducing insecurity about outcome.

An interesting finding was that before commencement of chemotherapy, the level of stress response symptoms of patient and partner was inversely related. When one spouse was reporting more stress response symptoms, the other reported less. This might be a psychological mechanism through which spouses want to protect one another from their own distress, a finding reported before in studies on couples facing cancer (29). Another possible interpretation might be that patients who expressed very low levels of distress were using denial, avoidance, or other repressive psychological mechanisms while their partners carried the psychological burden of stress. A patient who expresses high distress may also allow his spouse to assume a stronger supportive role, and thus reduce her expression of stress.

In line with the medical trajectory, physical functioning of patients was worst after completion of chemotherapy. As a consequence of chemotherapy, many patients still experience adverse side effects, including fatigue and a sense of physical exhaustion. Surprisingly, physical functioning of patients was better than that of the reference group before start of chemotherapy and one year later. The first measurement occurred shortly after removal of the affected testicle, and patients may have experienced physical relief after the initiation of treatment. It may also be that age contributed to the difference found between the patient group and the reference group. Younger age is associated with better physical functioning (27), and the mean age of the patients in this study was somewhat more than ten years lower than that of the reference group. There may have been other differences from the reference group as well, such as physical activity, SES, etcetera. Partners' physical functioning did not change over the year but they also experienced better physical functioning than the reference group before and after chemotherapy. In an earlier study we found that partners of testicular cancer survivors reported better physical functioning than a reference group of women even years after diagnosis (32). Partners of testicular cancer patients may have changed the evaluation of their own health in a positive way after witnessing the diagnosis and treatment of a life threatening illness.

In patients, social functioning was worst immediately after completion of chemotherapy, and in spouses before start of chemotherapy. Before start of chemotherapy, both partners reported worse social functioning as compared to the reference groups. Before chemotherapy starts, couples are probably overwhelmed by the implications of a cancer diagnosis, and

focusing on the treatment to come rather than on being socially active as usual. As a consequence of chemotherapy, patients may still suffer from negative side effects like fatigue and impaired physical functioning, which in turn may affect their social functioning. Social functioning in patients and partners was positively related after completion of chemotherapy, meaning that when one partner experienced better social functioning the other did also. Couples had comparable social functioning to that of the reference groups one year after diagnosis; they seem to have returned to their usual social activities. This finding is in line with studies on testicular cancer survivors that show little or no change in social contacts and work activities (6;33).

Mental health of patients improved over the year. It was poorer than that of men in the reference group only before start of chemotherapy. Mental health of partners was comparable throughout the year and to that of a reference group of women, despite the high level of stress response symptoms they reported before start of chemotherapy. Stress response symptoms apparently are a different expression of mental functioning, and may be encapsulated or separated out.

It appeared that functioning in couples facing testicular cancer was not similar in patient and partners. Testicular cancer patients showed u-shaped trajectories of stress response symptoms, physical and social functioning, a pattern seemingly following the medical trajectory they had undergone. Mental health of patients improved over the year. Spouses reported a decline in stress response symptoms and an improvement in social functioning, but no change in physical functioning or mental health over the year. Differences between patients and partners were also noticeable in stability of functioning. In patients, earlier levels of stress response symptoms were strongly predictive of later levels while less individual stability was found with regard to physical and social functioning and to mental health. Partners reported less individual stability in stress response symptoms over time, although individual stability was found between T2 and T3. However, partners were individually highly consistent in their reports of physical functioning and somewhat less strong in mental health and social functioning. In addition, correlations between the functioning of patients and partners were moderate to very low. We also found that at the second and third measurement time, there were no couples in which both the patient and the partner reported clinically elevated levels of stress response symptoms. This finding confirms the lack of correspondence in functioning between patient and partner.

These findings support recent studies that found different adjustment patterns for patients and partners, and a lack of correspondence in functioning (19;20). Research is needed to examine if these different reaction patterns to a cancer diagnosis affect the marital relationship.

This study has some limitations. First, the possibility of including couples was limited because testicular cancer has a low incidence. Besides, no information was available on the functioning of couples who declined to participate. They may have been those who were functioning

best or worst, thus biasing the results in either direction. Because of the limited sample size, variables that measure relationship aspects were not included in this study. In a previous retrospective study on testicular cancer, factors identified as important for couple adjustment like good communication, spousal support, and marital satisfaction all appeared to facilitate better functioning (34). These moderating factors in adjustment of both patient and spouse deserve to be studied prospectively in the future.

In summary, this study was a prospective exploration of functioning in couples facing testicular cancer during the first year after the diagnosis. Patients confronted with disseminated testicular cancer and their partners reacted differently to this stressor. Clinically elevated stress response levels were present in one third of patients and half of the partners before start of chemotherapy. Patients reported worst mental health before start of chemotherapy, and worst physical and social functioning immediately after completion of chemotherapy. Partners reported an improvement in social functioning, and no change in physical functioning and mental health over the year. Quality of life of patients and partners was comparable to that of the reference groups a year after start of chemotherapy, patients even reported better physical functioning at that time. These findings support earlier retrospective studies in testicular cancer survivors and their spouses that also reported few long-term effects in psychosocial functioning in the group overall, but that identified a small group that remains distressed (16;34;35). Little correspondence was found in the functioning of the partners. Clinicians can be reassured that the effect of disseminated testicular cancer on the quality of life of patients and their partners seems to be temporary. However, a minority does seem to need clinical attention for stress response symptoms.

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