

Prevalence, Changes in and Correlates of Fatigue in the First Year after Diagnosis of Testicular Cancer

JOKE FLEER¹, DIRK T. SLEIJFER², HARALD J. HOEKSTRA¹,
MARRIT A. TUINMAN¹ and JOSETTE E.H.M. HOEKSTRA-WEEBERS^{3,4}

¹Department of Surgical Oncology, ²Department of Medical Oncology and
³Departments of Psychosocial Services and Health Psychology,

University Medical Center Groningen, P.O. Box 30.001, 9700 RB Groningen;

⁴Comprehensive Cancer Center North-Netherlands, P.O. Box 330, 9700 AH Groningen, The Netherlands

Abstract. *Aim: To examine fatigue among testicular cancer patients during the first year after diagnosis. Patients and Methods: Fifteen patients treated with orchidectomy (group 1) and 37 treated with orchidectomy plus chemotherapy (group 2) were assessed within 1 month after orchidectomy, and 3 and 12 months later. Fatigue, sociodemographics, anemia, testosterone levels and trait anxiety were assessed. Results: At T1 and T3, the groups reported similar levels of fatigue. Increased fatigue was found in group 2 at T2. A continuing decrease in fatigue was found in group 1. At T3, patients reported similar levels of fatigue as healthy individuals. Older age, trait anxiety and earlier levels of fatigue were predictive of fatigue, while anemia and testosterone levels were not. Conclusion: Fatigue seems not to be an enduring problem for testicular cancer patients, with treatment only having an impact on fatigue levels shortly after treatment. Highly anxious patients and those who were fatigued after orchidectomy might benefit from a multidisciplinary intervention.*

Testicular cancer affects men between 15 and 45 years, when they are in the prime of their life. Since the introduction of cisplatin-based polychemotherapy in the late 1970s, (disseminated) testicular cancer has become one of the most curable malignancies. Almost 90% of the testicular cancer patients can be cured with existing treatment modalities (1, 2). Consequently, these men will have to face a possible sequel of disease and treatment. Fatigue is one

of the most prevalent sequels of cancer and its treatment and it is known for its potential negative effects on the wellbeing of patients (3).

Fatigue is considered to be a subjective and multi-dimensional construct with several types of expression. For one person fatigue may express itself as physical exhaustion (physical fatigue), in another as diminished concentration and attention (cognitive fatigue), or as a lack of motivation and interest (mental fatigue) (4). Therefore, it is important to assess fatigue multidimensionally.

The prevalence of fatigue in patients under treatment for different types of cancer varies between 25 and 75%. It remains a problem for one-third of the patients for months, or even years, after treatment completion (4). Few studies have examined the prevalence and course of fatigue in testicular cancer patients. A pilot study measured the course of fatigue before, during and after chemotherapy in 16 testicular cancer patients, but this study did not use a multidimensional measurement instrument. At all time-points, testicular cancer patients reported low levels of fatigue, and these levels of fatigue did not change over time (5). One cross-sectional study assessed the prevalence of fatigue in testicular cancer survivors using a multi-dimensional questionnaire. The results showed that 16% of the survivors experienced mental and physical fatigue. Testicular cancer survivors younger than 30 years of age experienced more fatigue than the same age cohort of the general population (6).

Not all patients develop cancer-related fatigue, but the etiology of fatigue is not well understood to date. It is assumed that the origin is multifactorial, so, among others, physical and psychological correlates have been studied (for overviews see e.g. (4, 7, 8)). Sociodemographics have rarely been found to relate to cancer-associated fatigue (4), but in general more fatigue is found in older and unmarried people, as well as in those with a lower social status and educational level (9). Fatigue has been associated with the

Correspondence to: J. Hoekstra-Weebers, Groningen University Medical Center, Departments of Psychosocial Services and Health Psychology, P.O. Box 30.001, 9700 RB Groningen, The Netherlands. Tel: +31-50-3614978, Fax: +31-50-3619326, e-mail: j.hoekstra-weebers@psb.umcg.nl

Key Words: Testicular cancer, cancer-related fatigue, anemia, testosterone, trait anxiety.

type of treatment (e.g. surgery, radiotherapy, chemotherapy) during treatment for cancer, but cancer-related characteristics were unrelated to off-treatment fatigue. Furthermore, associations with several physical and psychosocial variables were found (4). Anemia and subnormal testosterone levels may be relevant physical contributors to fatigue in testicular cancer patients.

Anemia may be caused by the cancer itself, but it can be aggravated by intensive treatment (10). Chemotherapy, and to a lesser extent orchidectomy, may lead to a decrease of free and total levels of serum testosterone (11-13), and fatigue is one of the symptoms that has been associated with hypogonadism (14). However, the link between fatigue and both anemia and subnormal testosterone levels has never been examined in testicular cancer patients.

Most research into the psychological correlates of fatigue has focused on the association between depression and fatigue (4). Depression was reported to predict fatigue in testicular cancer survivors, but anxiety was found to be a more important contributory factor (6). People differ in their proneness toward experiencing anxiety (15), and it might be that this personality trait modifies the sensitivity to fatigue. Previous research has shown that cancer patients with an anxious disposition pay more attention to physical sensations, such as fatigue, than less anxious patients (16, 17). Furthermore, a recent study has confirmed the association between trait anxiety and fatigue in breast cancer patients (18). Therefore, it would be interesting to further explore the relationship between trait anxiety and cancer-related fatigue in testicular cancer.

The aim of the current study was to: (a) examine the effects of time and treatment modality on the levels of fatigue reported by testicular cancer patients during the first year after diagnosis; (b) compare levels of fatigue of testicular cancer patients with a reference group of Dutch people without a history of cancer; (c) investigate relationships between fatigue on the one hand and sociodemographics, anemia and serum testosterone levels on the other hand. Because it has been suggested that the degree of fatigue before the start of treatment may be one of the strongest predictors of post-treatment fatigue (19), the relationship between earlier and later levels of fatigue were also investigated; (d) investigate the concurrent and prospective contribution of trait anxiety on fatigue.

Patients and Methods

Participants. Patients diagnosed with a stage I or with disseminated non-seminomatous testicular tumor were eligible for this study. All patients received their diagnosis after the surgical removal of the testicle (orchidectomy). After orchidectomy, the patients were clinically staged, to establish the presence of metastases. Patients without metastases (stage I) were closely monitored in follow-up and were informed about their high cure rate of approximately

99%. Patients with metastases received chemotherapy and, based on their prognostic classification, they were informed about their cure rates (varying from 50-90%). After chemotherapy was completed, all chemotherapy-treated patients were restaged. The restaging procedure consisted of measurement of serum tumor markers and CT scanning of the chest and abdomen. Patients without biochemical or radiological abnormalities were considered to have reached a complete remission.

All eligible patients, who consecutively attended the University Medical Center Groningen (UMCG) in The Netherlands for treatment between April 2001 and March 2004, were approached. Exclusion criteria were age younger than 18 years at study entry, insufficient command of the Dutch language, and previous treatment for cancer. Twelve (17%) of the 71 patients approached refused to participate. Of the 59 patients who completed the first assessment, 4 did not complete the second questionnaire. Three of these dropouts refused further participation and 1 was too ill to complete the questionnaire. Of the 55 patients who completed the second assessment, 1 patient died before the third assessment. Two patients dropped out, because they had to receive additional treatment. The final group included 52 patients, of whom 15 (28.8%) were treated with orchidectomy alone, and 37 (71.2%) with orchidectomy and cisplatin-based chemotherapy. The patients treated with chemotherapy received 4 courses of cisplatin, etoposide and bleomycin, every 3 weeks.

Procedure. The study was introduced to the patients after orchidectomy had been performed and written informed consent was obtained. Participants with a stage I non-seminoma received a questionnaire at the following 3 time points: within 1 month after orchidectomy (T1), 3 months after T1 (T2) and 1 year after T1 (T3). Patients with disseminated non-seminoma received a questionnaire at the following 3 time-points: after orchidectomy and before the start of chemotherapy (T1), after chemotherapy, which is approximately 3 months after T1 (T2), and 1 year after T1 (T3).

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, marital status and employment status. The 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 consisted of the categories 'not employed for wages' (consisting of students, being unemployed, being unable to work and being retired) and 'employed for wages'.

Fatigue: Fatigue was assessed with the Multiple Fatigue Inventory (MFI-20), which is a self-report questionnaire consisting of 5 scales, each including 5 items: general fatigue, physical fatigue, reduced activity, reduced motivation and mental fatigue. The psychometric properties of this questionnaire have been found to be good (20). In the present study, internal consistency of the subscales varied between $\alpha=0.76$ and $\alpha=0.93$ for the 3 measurement times of the group of testicular cancer patients. Smets *et al.* (21) have reported data for the MFI-20 from an unselected group of 139 healthy Dutch individuals (male: 44%, mean age: 46 ± 16 years, married/ cohabiting: 64%), and this group was used as reference.

Anemia: The presence of anemia was determined using the guidelines of the Common Toxicity Criteria, version 3 (22). An Hb level >8.7 mmol/L indicates no anemia, 6.2-8.6 mmol/L grade 1 anemia, 4.9-6.1 mmol/L grade 2 anemia, 4.0-4.8 mmol/L grade 3 anemia and <4.0 mmol/L grade 4 anemia. Hemoglobin levels (Hb) were only determined in patients treated with orchidectomy plus chemotherapy ($n=37$).

Testosterone serum: Testosterone levels were considered as subnormal when the total testosterone level was less than 10 nmol/L (11). Total testosterone was measured using radioimmunoassay (Packard 1500/1600/2700, PerkinElmer, Groningen, The Netherlands). These data were only assessed in patients treated with chemotherapy. Three patients were excluded because both testicles were removed and consequently they received testosterone replacement therapy. Therefore, data were available for 34 patients.

Trait anxiety: Trait anxiety was measured with the Dutch version of the State-Trait Anxiety Inventory trait form (STAI-t) at T1(15, 23). The STAI-t is a psychometrically sound 20-item self-report measure of anxiety proneness. The items have 4 response categories, ranging from 'not at all'(1) to 'very much so'(4), resulting in scores from 20-80. In the present study, the internal consistency (Cronbach alpha) of this scale was 0.93.

Statistical analyses. Repeated measures analysis of variance was used to examine changes in levels of fatigue, with type of treatment (orchidectomy alone *versus* orchidectomy plus chemotherapy) as a between-groups factor. Mann-Whitney tests were used to compare men treated with orchidectomy alone with men treated with orchidectomy and chemotherapy. Independent *t*-tests were used to test differences between testicular cancer patients at T1 and T3 and individuals without a history of cancer. Descriptive statistics, Pearson correlations, *t*-tests and Mann-Whitney tests were used to examine relationships between fatigue and sociodemographics, anemia, testosterone and earlier levels of fatigue. A Pearson correlation coefficient lower than 0.30 indicates a poor relationship, a coefficient between 0.30 and 0.50 a moderately strong relationship, and a coefficient higher than 0.50 a strong relationship (24).

The predictive effect of trait anxiety on fatigue was examined concurrently (within time, T1 trait anxiety and T1 fatigue), and prospectively (T1 trait anxiety and T2 and T3 fatigue, controlling for T1 fatigue). By statistically controlling for levels of the dependent variable (*i.e.* fatigue) at T1, inferences can be made about the direction of the causal influence.

Results

Descriptives. The mean age of the respondents was 28.7 years, ranging from 18 to 44. The educational level completed varied from primary school to university degree, with a mean educational level of 4.0 (SD=1.3). More than half of the patients were married or cohabiting (59.6%), the rest were single. Most patients were employed for wages (78.8%).

Fatigue during the first year after diagnosis for testicular cancer: effects of time and type of treatment. Repeated measures analyses of variance showed a significant time

effect in physical fatigue, reduced activity and mental fatigue. Furthermore, significant interactive effects of time and type of treatment were found in all subscales, except for reduced motivation, which signifies that levels of fatigue changed over time in different ways for the groups. Inspection of the mean scores in the orchidectomy plus chemotherapy group showed that levels of fatigue increased from T1 to T2, and decreased from T2 to T3. A continuous decrease from T1 to T3, or a decrease from T1 to T2 followed by stabilization was found for the orchidectomy group (Table I). No significant effect of type of treatment was found (designated as 'group' in Table I), indicating no significant differences between the means of the 2 groups on the fatigue subscales at the different measurement times.

Because interactive effects were found and the groups were small, it was decided to compare the means of the orchidectomy and orchidectomy plus chemotherapy groups at the different measurement times. Mann-Whitney *U*-tests showed that the orchidectomy plus chemotherapy group reported significantly more physical fatigue and reduced activity at T2 than the patients who had undergone an orchidectomy only (Table I).

Comparison of levels of fatigue of testicular cancer patients shortly after orchidectomy and one year later with those of individuals without a history of cancer. Because the mean scores of the orchidectomy group and orchidectomy plus chemotherapy group did not differ significantly at T1 and T3, *t*-tests were performed with the total patient group. Analyses showed that testicular cancer patients reported significantly higher levels of reduced activity ($t=3.34$, $p=0.001$) and mental fatigue ($t=2.91$, $p=0.004$) at T1. At T3, the levels of fatigue of testicular cancer patients did not differ from those of healthy individuals (Table II).

Correlates of fatigue. Sociodemographics: At T1, age correlated significantly with reduced motivation ($r=0.32$, $p<0.05$). At T2, a significant correlation was found between age and all subscales of the MFI, except for mental fatigue ($r=0.29$ to $r=0.36$, $p<0.05$). At T3, age correlated significantly with general fatigue ($r=0.35$, $p<0.05$) and reduced motivation ($r=0.59$, $p<0.001$). All correlations were positive and moderately strong to strong, indicating that the older the patient the more fatigue he experienced. The only significant relationship found between educational level and fatigue was at T3. More highly educated patients reported more general ($r=0.30$, $p<0.05$) and physical fatigue ($r=0.29$, $p<0.05$). Marital status and employment status were not significantly related to fatigue.

Anemia: At T1, only 1 chemotherapy-treated patient had a grade 3 level of anemia, and at T2, 2 patients had a grade 2 level of anemia. The remaining patients were not or slightly anemic (grade 1 anemia) at any one of the 3 time-points. The

Table I. Means on the MFI-20 subscales and longitudinal analyses of fatigue.

MFI-20 subscale ^a		T1	T2	T3	Test of overall trend			
		Mean (SD)	Mean (SD)	Mean (SD)	Effect	F	p	
General fatigue	orchidectomy	11.0 (4.8)	9.7 (4.5)	10.3 (4.2)	Time	2.30	0.10	
	chemotherapy	10.2 (4.4)	12.5 (4.8)	8.9 (4.8)	Group	0.003	0.87	
					Interaction	5.09	0.008	
	Physical fatigue	orchidectomy	10.5 (4.3)	8.5 (4.5)	8.7 (4.4)	Time	5.96	0.004
		chemotherapy	9.4 (4.5)	13.0 (4.9)**	7.9 (4.4)	Group	0.54	0.47
					Interaction	9.45	<0.001	
	Reduced activity	orchidectomy	11.1 (5.1)	8.9 (4.6)	8.3 (3.5)	Time	11.00	<0.001
		chemotherapy	11.2 (4.5)	12.2 (4.1)*	7.6 (3.7)	Group	0.85	0.36
					Interaction	3.93	0.02	
	Reduced motivation	orchidectomy	8.1 (2.8)	7.0 (2.8)	7.1 (2.1)	Time	1.29	0.28
		chemotherapy	8.1 (4.3)	8.2 (2.7)	7.4 (3.5)	Group	0.60	0.44
					Interaction	0.68	0.41	
	Mental fatigue	orchidectomy	11.5 (5.3)	8.9 (4.2)	7.8 (3.7)	Time	6.72	0.002
		chemotherapy	10.1 (4.3)	10.5 (4.9)	9.5 (4.7)	Group	0.27	0.61
					Interaction	4.64	0.01	

^ahigher score indicates more fatigue

Mann-Whitney U-tests orchidectomy versus orchidectomy plus chemotherapy: *p≤0.05, **p≤0.01

group of patients with anemia was too small to investigate the effect on fatigue. However, the mean scores on the MFI-20 of the 3 patients with a grade 2 or 3 level of anemia fell within the range of mean scores of the other patients.

Testosterone: Only 1 patient had a testosterone level less than 10 nmol/L at T1. At T2 and T3, none of the patients had testosterone levels less than 10 nmol/L. Therefore, we could not investigate the effect of testosterone on fatigue. Yet, the mean scores on the subscales of the MFI-20 of the patient with an initially low testosterone level fell within the range of scores of the other patients.

Earlier levels of fatigue: Pearson's product moment correlation coefficients were significant between the different measurement times, ranging from 1 poor relationship to 6 moderately strong and 8 strong relationships (Table III). High correlation coefficients indicate consistency between the measurement times, so individuals were quite stable in their reports of levels of fatigue over time. They were least stable in their reports on the subscale of reduced activity.

Concurrent relationship between trait anxiety and fatigue: Trait anxiety correlated positively with all fatigue subscales at T1. The lowest, although moderately strong, correlation was found between trait anxiety and reduced motivation. The strongest relationship was found between trait anxiety and mental fatigue (Table III).

Prospective effect of trait anxiety on fatigue: After controlling for fatigue at T1, only a significant relationship between trait anxiety and reduced activity at T2 was found. In contrast, trait anxiety was significantly associated with 4/5

Table II. Means and standard deviations of testicular cancer patients at T1 and T3 (n=49) and individuals without a history of cancer (n=139; Smets et al., 1998).

	T1	T3	Reference group
	Mean (SD)	Mean (SD)	Mean (SD)
General fatigue	10.4 (4.4)	9.3 (4.6)	9.9 (5.2)
Physical fatigue	9.7 (4.5)	8.1 (4.4)	8.8 (4.9)
Reduced activity	11.2 (4.6)**	7.8 (3.6)	8.7 (4.6)
Reduced motivation	8.1 (3.9)	7.3 (3.1)	8.2 (4.0)
Mental fatigue	10.5 (4.6)*	9.0 (4.5)	8.3 (4.8)

T1 versus reference group: *p≤0.01, **p≤0.001

subscales at T3. The exception was a non-significant relationship between trait anxiety and reduced motivation (Table III). These findings indicate little causal effect of trait anxiety on fatigue at T2, whereas at T3 a causal effect of trait anxiety on most subscales of fatigue was found.

Discussion

The current study is the first to examine, with a multidisciplinary measurement instrument, the prevalence, changes in and correlates of fatigue among testicular cancer patients treated during the first year after orchidectomy.

The prevalence of fatigue changed over time and varied between the treatment groups. At the first assessment, shortly

Table III. Correlations between earlier and later levels of fatigue and between trait anxiety (STAI-t) and fatigue concurrently and prospectively.

	T1-T2	T2-T3	T1-T3	Concurrent	Prospective	
	r	r	r	STAI-t and T1 fatigue r	STAI-t and T2 fatigue <i>Partial r^a</i>	STAI-t and T3 fatigue <i>Partial r^a</i>
General fatigue	0.40**	0.51***	0.47***	0.51***	0.16	0.32*
Physical fatigue	0.30*	0.46***	0.52***	0.54***	0.20	0.33*
Reduced activity	0.27*	0.37**	0.36**	0.54***	0.34*	0.32*
Reduced motivation	0.52***	0.52***	0.56***	0.46***	0.17	0.24
Mental fatigue	0.61***	0.73***	0.55***	0.64***	0.19	0.31*

^acontrolling for fatigue at T1

* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$

after hearing the diagnosis and the surgical removal of the affected testicle, the orchidectomy and orchidectomy plus chemotherapy group reported similar levels of fatigue. They reported significantly more reduction in activity and mental fatigue than individuals without a history of cancer. Both the physical recovery from the operation and anesthesia, and the distressing emotions that follow from hearing a cancer diagnosis are likely to have contributed to these higher levels of fatigue. Three months later, the orchidectomy group reported lower levels of fatigue, whereas the orchidectomy plus chemotherapy-treated patients experienced increased fatigue. This increase may be explained by the chemotherapy treatment received by these patients. Patients in this group were assessed immediately after completion of chemotherapy and chemotherapy is known to cause fatigue (4, 7). One year after orchidectomy, both the orchidectomy and orchidectomy plus chemotherapy groups reported similar levels of fatigue as individuals without a history of cancer. These findings suggest that fatigue seems not to be an enduring problem for the majority of testicular cancer patients, irrespective of the treatment received. Apparently, treatment has an impact on fatigue only shortly after orchidectomy and completion of chemotherapy. This finding elucidates why previous studies did not find an effect of treatment modality on fatigue in long-term survivors of testicular cancer (6, 25).

The relationships between fatigue and sociodemographics, physical factors and trait anxiety were studied among the testicular cancer patients. Of the sociodemographics, age was related to at least 1 of the fatigue subscales at all measurement times. Similar to our study, increased fatigue with age has been found in both the general population (9, 26) and cancer populations (6, 27, 28). It should be noted that the testicular cancer patients were relatively young compared to the reference group. So, it is possible that, if we had compared the testicular cancer patients with people of their own age, higher levels of fatigue would have been found for the testicular cancer patients.

Associations with marital and social status have also been reported in the general population (9), but we could not identify such relationships in the current study. Furthermore, our finding that a higher educational level was related to physical fatigue 1 year after diagnosis disagreed with findings in the general population, showing that shorter education was associated with higher fatigue scores (9).

The occurrence of both anemia and hypogonadism was rare in our study population. The majority of patients had hemoglobin levels in the normal or in the mild anemic range and normal testosterone levels at all measurement times. This is consistent with previous reports that only a minority of testicular cancer patients will develop moderate or severe anemia (29) or hypogonadism (11-13). Both the patients with anemia and the 1 hypogonadic patient reported fatigue levels within the range of the whole group of testicular cancer patients. Studies with large sample sizes are needed to gain definitive insight into the impact of anemia and hypogonadism on fatigue levels.

Earlier levels of fatigue were predictive of later levels of fatigue. In broad terms, those reporting higher levels of fatigue after orchidectomy also reported higher levels of fatigue 3 months and 1 year later. Similar findings have been reported before (3, 30). This stresses the importance of identifying fatigued individuals early on in the disease trajectory to reduce post-treatment fatigue, because the longer fatigue lasts, the more it will disrupt the daily lives of patients (31, 32).

Testicular cancer patients with a more anxious disposition reported more fatigue after orchidectomy. Prospective analyses showed that trait anxiety had a predictive effect only in the subscale of reduced activity at the second measurement time, suggesting that, at this time-point, other variables are more important for the prediction of fatigue. The greater percentage of our sample (71%) consisted of patients treated with orchidectomy plus chemotherapy, so it is possible that chemotherapy-related

side-effects outweighed the impact of trait anxiety. Unfortunately, our sample size was too small to reliably investigate this hypothesis.

Interestingly, 1 year after orchidectomy, trait anxiety had a significant causal effect on all fatigue subscales. Research has shown that both highly anxious individuals (33) and chronically fatigued individuals (34, 35) use maladaptive strategies, such as avoidance coping, relatively often. Avoidance coping strategies lead people into activities or mental states (such as withdrawal and rumination) that keep them from directly addressing problems (36). So, the highly anxious testicular cancer patient might, for example, cope by avoiding physical exercise, which is known for its physical and psychological benefits (*e.g.* (37, 38)). Further research is needed to clarify the relationships between coping strategies, trait anxiety and fatigue among testicular cancer patients and survivors, especially because coping strategies have rarely been studied in relation to cancer-related fatigue (39).

Conclusion

Based on the results of the current study, it can be concluded that treatment for testicular cancer has an impact on levels of fatigue mainly in the short-term. Testicular cancer patients did experience more fatigue immediately after orchidectomy and, for those who received chemotherapy, following completion of chemotherapy. One year after orchidectomy, patients treated with orchidectomy alone as well as those treated with orchidectomy and chemotherapy reported levels of fatigue comparable to those of individuals without a history of cancer. Older age was related to increased fatigue. Earlier levels of fatigue were predictive of later levels of fatigue. Furthermore, concurrent and causal relationships were found between trait anxiety and fatigue. Older testicular cancer patients, those who already report being fatigued shortly after orchidectomy and those with a more anxious disposition, might benefit from a multidisciplinary intervention that focuses on physical exercise training and the strengthening of coping strategies to effectively reduce fatigue. A multidisciplinary approach for fatigue seems relevant, because when increased levels of fatigue were found in this study, it was found in all domains.

Acknowledgements

This research was supported by a grant from the Dutch Cancer Society, no. RUG 99-2130.

References

- Bosl GJ and Motzer RJ: Testicular germ-cell cancer. *N Engl J Med* 337: 242-253, 1997.
- Dearnaley D, Huddart R and Horwich A: Regular review: managing testicular cancer. *BMJ* 322: 1583-1588, 2001.
- Smets EMA, Visser MRM, Garssen B, Frijda NH, Oosterveld P and De Haes JCJM: Understanding the level of fatigue in cancer patients undergoing radiotherapy. *J Psychosom Res* 45: 277-293, 1998.
- Servaes P, Verhagen C and Bleijenberg G: Fatigue in cancer patients during and after treatment: prevalence, correlates and interventions. *Eur J Cancer* 38: 27-43, 2002.
- Trask PC, Paterson AG, Fardig J and Smith DC: Course of distress and quality of life in testicular cancer patients before, during, and after chemotherapy: results of a pilot study. *Psycho-Oncology* 12: 814-820, 2003.
- Fossa SD, Dahl AA and Loge JH: Fatigue, anxiety, and depression in long-term survivors of testicular cancer. *J Clin Oncol* 21: 1249-1254, 2003.
- Tavio M, Milan I and Tirelli U: Cancer-related fatigue (Review). *Int J Oncol* 2: 1093-1099, 2002.
- Stasi R, Abriani L, Beccaglia P, Terzoli E and Amadori S: Cancer-related fatigue – evolving concepts in evaluation and treatment. *Cancer* 98: 1786-1801, 2003.
- Watt T, Groenvold M, Bjorner JB, Noerholm V, Rasmussen NA and Bech P: Fatigue in the Danish general population. Influence of sociodemographic factors and disease. *J Epidem Community Health* 54: 827-833, 2000.
- Pujade-Lauraine E and Gascon P: The burden of anaemia in patients with cancer. *Oncology* 67(Suppl.1): 1-4, 2004.
- Nuver J, Smit AJ, Wolffenbuttel BH *et al*: The metabolic syndrome and disturbances in hormone levels in long-term survivors of disseminated testicular cancer. *J Clin Oncol* 23: 3718-3725, 2005.
- Nord C, Bjoro T, Ellingsen D *et al*: Gonadal hormones in long-term survivors 10 years after treatment for unilateral testicular cancer. *Eur Urol* 44: 322-328, 2003.
- Brennemann W, Stoffel-Wagner B, Helmers A, Mezger J, Jager N and Klingmuller D: Gonadal function of patients treated with cisplatin based chemotherapy for germ cell cancer. *J Urol* 158: 844-850, 1997.
- Shores MM, Sloan KL, Matsumoto AM, Mocerri VM, Felker B and Kivlahan DR: Increased incidence of diagnosed depressive illness in hypogonadal older men. *Arch Gen Psych* 61: 162-167, 2004.
- Spielberger D, Gorsuch L and Lushene E: STAI Manual. Palo Alto: Consulting Psychologists Press, 1970.
- Stark D, Kiely M, Smith A, Morley S, Selby P and House A: Reassurance and the anxious cancer patient. *Br J Cancer* 91: 893-899, 2004.
- Cameron LD, Leventhal H and Love RR: Trait anxiety, symptom perceptions, and illness-related responses among women with breast cancer in remission during a tamoxifen clinical trial. *Health Psychol* 17: 459-469, 1998.
- Sugawara Y, Akechi T, Okuyama T *et al*: Occurrence of fatigue and associated factors in disease-free breast cancer patients without breast cancer. *Support Care Cancer* 13: 628-636, 2005.
- Smets EMA, Visser MRM, Willems-Groot AFMN *et al*: Fatigue and radiotherapy: (A) experience in patients undergoing treatment. *Br J Cancer* 78: 899-906, 1998.
- Smets EMA, Garssen B, Bonke B and Dehaes JCJM: The Multidimensional Fatigue Inventory (Mfi). Psychometric qualities of an instrument to assess fatigue. *J Psychosom Res* 39: 315-325, 1995.

- 21 Smets EMA, Visser MRM, Willems-Groot AFMN, Garssen B, Schuster-Uitterhoeve ALJ and De Haes JCJM: Fatigue and radiotherapy: (B) experience in patients 9 months following treatment. *Br J Cancer* 78: 907-912, 1998.
- 22 Common Toxicity Criteria, Version 3. National Cancer Institute, 4-7-2005.
- 23 Ploeg HM van der, Defare PB and Spielberger CD: Handleiding bij de Zelf-Beoordelings Vragenlijst (ZBV). Lisse: Swets Test Publishers, 2000.
- 24 Cohen J: Statistical Power Analysis for the Behavioral Sciences. 2nd edition. Hillsdale NJ (ed.): Erlbaum, 1988.
- 25 Joly F, Heron JF, Kalusinski L *et al*: Quality of life in long-term survivors of testicular cancer: a population-based case-control study. *J Clin Oncol* 20: 73-80, 2002.
- 26 Loge JH, Ekeberg O and Kaasa S: Fatigue in the general Norwegian population: normative data and associations. *J Psychosom Res* 45: 53-65, 1998.
- 27 Bower JE, Ganz PA, Desmond KA, Rowland JH, Meyerowitz BE and Belin TR: Fatigue in breast cancer survivors: occurrence, correlates, and impact on quality of life. *J Clin Oncol* 18: 743-753, 2000.
- 28 Loge JH, Abrahamsen AF, Ekeberg and Kaasa S: Fatigue and psychiatric morbidity among Hodgkin's disease survivors. *J Pain Symptom Manage* 19: 91-99, 2000.
- 29 Weissbach L, Bussar-Maatz R, Flechtner H, Pichlmeier U, Hartmann M and Keller L: RPLND or primary chemotherapy in clinical stage IIA/B nonseminomatous germ cell tumors? Results of a prospective multicenter trial including quality of life assessment. *Eur Urol* 37: 582-594, 2000.
- 30 Maliski SL, Kwan L, Orecklin JR, Saigal CS and Litwin MS: Predictors of fatigue after treatment for prostate cancer. *Urology* 65: 101-108, 2005.
- 31 Irvine DM, Leslie V, Graydon JERN and Bubela N: Fatigue in women with breast cancer receiving radiation therapy. *Cancer Nurs* 21: 127-135, 1998.
- 32 Molassiotis A and Chan CWH: Fatigue patterns in Chinese patients receiving radiotherapy. *Eur J Oncol Nurs* 8: 334-340, 2004.
- 33 Deisinger JA, Cassisi JE and Whitaker SL: Relationships between coping style and PAI profiles in a community sample. *J Clin Psychol* 52: 303-310, 1996.
- 34 Nijs J, De Meirleir K and Duquet W: Kinesiophobia in chronic fatigue syndrome: assessment and associations with disability. *Arch Phys Med Rehab* 85: 1586-1592, 2004.
- 35 Afari N, Schmaling KB, Herrell R, Hartman S, Goldberg J and Buchwald DS: Coping strategies in twins with chronic fatigue and chronic fatigue syndrome. *J Psychosom Res* 48: 547-554, 2000.
- 36 Holahan CJ and Moos RH: Personal and contextual determinants of coping strategies. *J Pers Soc Psychol* 52: 946-955, 1987.
- 37 Dimeo F, Bertz H, Finke J, Fetscher S, Mertelsmann R and Keul J: An aerobic exercise program for patients with haematological malignancies after bone marrow transplantation. *Bone Marrow Transpl* 18: 1157-1160, 1996.
- 38 Dimeo FC: Effects of exercise on cancer-related fatigue. *Cancer* 92: 1689-1693, 2001.
- 39 Jong N de, Courtens AM, Huijter Abu-Saad H and Schouten HC: Fatigue in patients with breast cancer receiving adjuvant chemotherapy: a review of the literature. *Cancer Nurs* 25: 283-297, 2002.

Received July 8, 2005

Accepted August 30, 2005