Sexual dysfunctions in men treated for testicular cancer – secondary publication

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ABSTRACT

Patients treated for testicular cancer have increased risk of ejaculatory, orgasmic and erectile dysfunction compared with healthy men. The underlying relations are unclear. This review describes sexual dysfunctions that are associated with various treatment modalities. A metaanalysis and 11 original works were examined. About one third of the patients experience one or more sexual problems in relation to the treatment. Only retroperitoneal surgery can cause a specific sexual dysfunction, namely loss of ejaculation ability or ejaculatory functioning. Psychosexual causes are important for understanding sexual dysfunctions in patients with testicular cancer.

This review describes the occurrence of sexual dysfunctions in testicular cancer patients based on the various treatment modalities, and it gives a summary of essential methodological details in selected literature.

With an incidence of approx. 300, testicular cancer is the most common form of cancer in Danish men in the age range 15-35 years [1]. The recovery rate is high, and the majority of the men resume a normal life at the end of the treatment.

Over the course of time there has been clinical and scientific interest in whether these men acquire sexual dysfunctions that are associated with their disease and treatment. There may be organic sexual dysfunctions as a result of the treatment and non-organic dysfunctions as a result of psychosexual changes associated with the disease. In studies, increased risk of certain sexual dysfunctions has been observed to a varying degree – but the picture is by no means clear. What has been clearer is that the patients feel that they receive too little information about what impact the treatment can have on their sexuality. [2].

In all cases the treatment of testicular cancer consists of orchiectomy of the affected testis, biopsy from the contralateral testis and subsequent staging. Patients without any signs of metastatic cancer do not receive any further treatment, but are monitored – the surveillance group. 20-30% of these patients will experience a relapse.

Patients with metastatic cancer are treated with chemotherapy (for 3-4 months) or – for a smaller group – solely with radiation treatment of the pelvic and retroperitoneal lymph nodes. After chemotherapy, in 25% of patients there will be residual tumours, which in most cases necessitate post-chemotherapy surgical resection of residual retroperitoneal tumor mass (RRRTM) and possibly supplementary chemotherapy [1].

A metaanalysis of controlled studies showed significantly increased risk of erectile dysfunction (ED) and ejaculatory dysfunction (EJD), and inhibited orgasm in testicular cancer patients compared with healthy men. EJD is not further defined in this context and may include premature and delayed ejaculation, absent/retrograde ejaculation and painful ejaculation. The analysis does not, however, describe the effect of the individual treatment modalities [3]. Furthermore, it is emphasized that investigations of this subject are characterized to a considerable degree by variation in design and instruments used, as well as many have poor methodological strength. Thus, in previous review articles it was not possible to draw definite conclusions on whether the individual treatment modalities for testicular cancer produce sexual dysfunctions as a result of an immediate or long term effect on the patient [3-6].

MATERIAL AND METHODS

This review is based on a metaanalysis by Jonker-Pool et al (JP) published in 2001 [7], relating sexual dysfunctions to the various treatment modalities. Moreover, this review is based on an updating literature search, performed via PubMed and psycINFO with the words: *testicular neoplasm, testicular cancer and sex, sexual functioning, sexual rehabilitation, erection, impotence, erectile dysfunction, ejaculation, orgasm, sexual desire* and *libido*.

This was followed by a critical evaluation of the original literature and a selection was made using following inclusion criteria: reflects current treatment modalities, identifiable treatment modalities, identifiable sexual dysfunctions, identifiable design and method and English or Danish language.

RESULTS OF THE LITERATURE SEARCH

JP's [7] metaanalysis comprises 29 retrospective and seven prospective studies conducting an analysis on sexual dysfunction at the various treatment modalities. The metaanalysis does not categorize the evidence of the included studies.

The updating literature search resulted in a total of 11 studies, which were published later than JP's analysis.

For closer examination in this article we selected four of the new articles and seven of those that were included in JP's analysis. The studies comprise four case-control studies, six cross-sectional studies and a single prospective study. Further characteristics of the selected studies can be seen in Table 1.

The main reason for literature being excluded was lag of differentiation between the various treatment modalities.

In the following the result of the examination of the literature is reviewed based on each individual treatment modalities. A synopsis of these results is presented in Table 2.

SURVEILLANCE GROUP

The prevalence of sexual dysfunctions in this group is only described scantily and no well-designed controlled studies have been conducted. The surveillance group is often used as a control group for other treatment modalities.

JP's metaanalysis is based on four studies, comprising a total of 108 surveillance patients. The analysis shows reduced sexual desire in 25%, ED in 7%, orgasmic dysfunction in 24%, EJD in 16%, reduced sexual activity in 11% and dissatisfaction with sex life in 8% [7]. The four studies have, between them, large variations in prevalence of sexual dysfunctions. One of the studies, which includes the largest population of 56 surveillance patients [15] and was selected for examination here (Table 1) shows considerably lower prevalence of sexual dysfunctions compared with the pooled data. 12% had reduced sexual desire, 2% ED, and 12% had reduced orgasmic sensation, and 7% reported greater dissatisfaction with sex life as a result of the treatment. None experienced absence of ejaculation [15].

The possibility of hormonal dysregulation as a result of orchiectomy proved to be unimportant for sexual function [1, 8].

Summary

Reduced sexual desire and orgasmic dysfunction is a particular bother for patients in the surveillance group. There are no somatic explanations for this. The results are, however, characterized by considerable variation, and there is no well-executed prospective investigation of the surveillance group.

RADIATION THERAPY

JP's metaanalysis of this group comprises nine studies with a total of 417 patients. The analysis showed reduced desire in 14%, ED in 25%, orgasmic dysfunction in 23%, EJD in 40%, reduced sexual activity in 29% and dissatisfaction with sex life in 16% of the men interviewed [7].

The selected studies have large variations in the reported prevalence of sexual dysfunctions in this group of men, where 19-22% experienced reduced sexual desire, 10-48% ED, 0-5% absence of ejaculation, 14-38% dissatisfaction with orgasm and 7-28% an unsatisfactory sex life [2, 9, 10, 12, 15, 17]. A varied picture was also seen compared with healthy controls. Some studies show increased frequency of reduced sexual desire, ED and reduced pleasure at orgasm [9, 12]. In other controlled studies it was found that sexual function was unchanged [10, 11]. Of the latter, the study by Incrocci et al in particular seems to be well-designed. Fourty-four patients in a well-defined age group (40-49 years) were studied, and each patient was matched with at least four healthy controls [10].

Table 1. Characteristics of selected studies describing sexual dysfunctions following treatment for testicular cancer.

Reference	Design	Population n (response)	Time-period for treatment	Follow-up average (standard deviation)	Evidence level[a]	Appearance of sexual dysfunction
van Basten et al, 1999 [8] JP Holland	Prospective SQ	CHEMO: 10 SURV: 11	1994-1998	t1 = before orchiectomy t2 = 6mdr. after orchiectomy t3 = 1year after orchiectomy	2	→, 1year after orchiectomy After CHEMO though was found temporary increased prevalence of ED, reduced sexual desire and orgasmic dysfunction[b]
Joly F. et al, 2002 [9] New France	Prospective NSQ	Total: 71 (83%) Control: 121 (50%) SURV: 6 RAD: 29 CHEMO: 12 RAD + CHEMO: 4 RPLND: 13 RRRTM: 9	1978-1993	11 year (5-20 year)	3	ED ↑, especially after RAD EJD ↑ after RPLND[c]
Incrocci L. et al, 2002 [10] New Holland	Case-control SQ	RAD: 44 (78%) Control: 185 (70%)	1989-1998	4.25 year (1 mth-10 year)	3	→ after RAD[c]
Cassileth BR et al, 1987 [11] JP USA	Case-control NSQ	RAD: 39 (58%)	Last 20 years	7.3 year (1-20 year)	3	→ after RAD Tendency for more sexual satisfaction among cases[c]
Tinkler S. et al, 1992 [12] JP Scotland	Case-control	RAD: 137 (62%) Control: 121 (35%)	1974-1988	8.9 year (2-17 year)	3	ED ↑, orgasmic dysfunction ↑, reduced sexual desire ↑ after RAD[c]
Böhlen D. et al, 2001 [13] New Switzerland	Cross-sectional NSQ	CHEMO: 49 (83%)	1985-1994	7.75 year (2.6-12.2 year)	3	→, 6 months after treatment After CHEMO though was found temporary reduced sexual desire and/or ED in 8%[d]
Huddart R.A. et al, 2005 [14] New UK	Cross-sectional SQ	Total: 680 (94%) SURV: 182 RAD: 175 CHEMO + RAD: 90 CHEMO: 292	1982-1992 (0-20 year)	10.2 year	3	Reduced sexual interest ↑ after CHEMO Reduced sexual pleasure ↑ after RAD[c]
Jonker-pool G. et al, 1997 [15] JP Holland	Cross-sectional NSQ	Total: 264 (78%) SURV: 59 RAD: 41 CHEMO: 42 RRRTM: 122	1977-1994	6.7 year (0.25-18 year)	3	All dysfunctions ↑ after RRRTM or CHEMO When controlling for age only ED ↑[c]
Caffo O. et al, 1999 [2] JP Italy	Cross-sectional SQ	RAD: 89 (69%) At regio paraaorta	1961-1995	10.25 year (1-41 year)	3	ED ↑ 11% Orgasmic dysfunction ↑ 13% Decreased sexual ability ↑ 12% Dissatisfaction with sex life ↑ 28%[d] Age was the only predictive factor for sexual dysfunctions
Hartman JT et al, 1999 [16] JP Germany	Cross-sectional NSQ	Total: 98 (78%) SURV: 7 RPLND: 13 CHEMO: 32 RRRTM: 42	1970-1993	12 year (2.8-25.6 year)	3	Loss of ejaculation ability ↑ after RPLND and RRRTM[c]
Arai et al, 1997 [17] JP Japan	Cross-sectional NSQ	Total: 85 (79%) SURV: 9 RAD: 42 CHEMO: 15 PKRTR: 19	1971-1993	7.7 year (1-21 year)	3	Loss of ejaculation ability ↑ after RRRTM[c]

SURV = surveillance; CHEMO = chemotherapy; RAD = radiation therapy; RRRTM = post-chemotherapy surgical resection of residual retroperitoneal tumor mass; RPLND = retroperitoneal lymph node dissection; NSQ = non-standardized questionnaire; SQ = standardized questionnaire; JP = included in Jonker-Pool's meta analysis [7]; New = published after Jonker-pool's analysis; ↑ = increased prevalence; → = unchanged prevalence. a) Oxford Centre for Evidence-based Medicine Levels of Evidence. b) Surveillance. c) Healthy control. d) Baseline (the patient controls for himself).

In a small number of studies the frequency of sexual problems during radiation therapy is compared with the frequency during the other treatment modalities. No statistically significant difference in frequency of sexual dysfunctions was found during radiation therapy [8, 14, 17]. However, in the study by Huddart et al significantly more men experienced reduced sexual pleasure compared to the surveillance patients. Though, the results had not been corrected for age and follow-up time [14].

In just one study, increased risk of ED was observed the higher the radiation dose applied on the retroperitoneal paraaortic lymph nodes (close to 3600 Rad) [18]. In other studies it is suggested that there may be damage to the small vessels and nerves that control penile blood supply [19]. It is doubtful, however, whether this finding is of any clinical significance, and more substantial studies on testicular cancer patients are needed.

Summary

A considerable number of patients treated with radiation therapy experience ED, and problems with orgasm and desire. A particular effect on erectile function is indicated in several studies, but the picture is unclear. Thus, it has not been possible to show that sexual dysfunctions occurring in connection with radiation therapy are due solely to the radiation therapy. Well-designed prospective studies of this subject are needed.

CHEMOTHERAPY

JP's metaanalysis of this group includes 160 patients described in six studies. The analysis shows reduced sexual desire in 25%, ED in 11%, orgasmic dysfunction in 28%, EJD in 28%, reduced sexual activity in 34% and dissatisfaction with one's own sexuality in 15% [7].

In three of the selected studies [8, 15, 16] (Table 1), which are included in JP's analysis, it is emphasized that the chemotherapy group experiences significantly more sexual dysfunctions (reduction of sexual activity, reduced desire, orgasmic dysfunction, inhibited ejaculation and ED) than the surveillance group [8, 15]. However, when corrected for age, only ED is significantly different [15], and the effect is shown to be transient in the prospective study, as it was shown that sexual function normalized to the surveillance level approximately one year after the treatment stopped [8]. In a more recent study of a larger group of chemotherapy patients (n = 292), significantly reduced sexual desire was only found in the surveillance group [14]. Similarly, in another more recent study, temporary reduced desire and/or ED were only found in 8% who received chemotherapy [13].

The isolated effect of chemotherapy treatment has not been investigated in comparison with healthy men.

No connection was found between ED and plasma testosterone or penile blood flow during chemotherapy [8]. There is some suggestion, however, that patients who get Raynaud's phenomenon as a side effect of chemotherapy also have a considerable increased risk of getting ED, which indicates that vascular aetiology is perhaps of importance [20].

Summary

After chemotherapy, an almost global effect on sexuality is seen in a considerable number of patients. There is some suggestion that this effect is only temporary, and it has not been possible to find any organic explanation for the effect.

POST-CHEMOTHERAPY SURGICAL RESECTION OF RESIDUAL RETROPERITONEAL TUMOR MASS

This treatment modality has not been investigated in comparison with healthy controls. In JP's metaanalysis [8] this treatment regimen was not examined separately, but dysfunctions were examined in 404 patients who received resection of residual retroperitoneal tu-

Table 2. Changes in sexual function following treatment for testicular cancer.

	Sexual problems compared to			
Treatment[a]	before the treatment (baseline)[b]		surveillance	healthy individuals
Surveillance	Reduced sexual desire	25%		?
	Orgasmic dysfunction	24%		?
	EJD	16%		?
	Reduced sexual activity	11%		?
	Dissatisfaction with sex life	8%		?
	ED	7%		?
Chemotherapy	Reduced sexual activity	34%	→	?
	Orgasmic dysfunction	28%	→	?
	EJD	28%	→	?
	Reduced sexual desire	25%	↑→	?
	Dissatisfaction with sex life	15%	→	?
	ED	11%	↑→	?
Radiation therapy	EJD	40%	→	→
	Reduced sexual activity	29%	→	→
	ED	25%	→	↑→
	Orgasmic dysfunction	23%	→	↑→
	Dissatisfaction with sex life	16%	→	→
	Reduced sexual desire	14%	→	↑→
RRRTM or RPLND + Chemotherapy	Orgasmic dysfunction	62%	↑ (also in comparison to CHEMO and RAD)	?
	EJD	40%	↑	?
	Reduced sexual activity	29%	↑	?
	Dissatisfaction with sex life	20%	↑	?
	Reduced sexual desire	13%	→ (also in comparison to CHEMO and RAD)	?
	ED	11%	→ (also in comparison to CHEMO or RAD)	?

SURV = surveillance; CHEMO = chemotherapy; RAD = radiation therapy; RRRTM = post-chemotherapy surgical resection of residual retroperitoneal tumor mass; RPLND = retroperitoneal lymph node dissection; EJD = ejaculatory dysfunction; ED = erective dysfunction; ↑ = increased prevalence; → = unchanged prevalence. a) All individuals are treated with unilateral orchiectomy. b) The prevalences are from Jonker-Pool's metaanalysis [7]. ?) Surveys do not exist.

mor mass (RRRTM) or chemotherapy and retroperitoneal lymph node dissection (RPLND), which is a dissection of retroperitoneal lymph nodes, which previously was carried out inter alia on those who nowadays are treated with surveillance. RPLND is no longer used in Denmark. In this group, 13% reports reduced desire, ED in 11%, orgasmic dysfunction in 22% , EJD in 62%, 29% have reduced sexual activity, and 20% are dissatisfied with their sexuality.

In three of the selected studies included in JP's analysis, it was found that RRRTM compared with the surveillance group had a significantly higher frequency of absence of ejaculation [15-17] and reduced sexual activity and sexual satisfaction [15]. Compared with chemotherapy or radiation therapy, absence of ejaculation was significantly more frequent, whereas no difference was seen in the frequency of other dysfunctions [15-17].

The reason why this treatment in particular leads to absence of ejaculation capacity is a complication associated with the actual intervention, because resection in the retroperitoneum may cause damage to retroperitoneal sympathetic nerve fibres and thus cause retrograde ejaculation [20].

Summary

Patients who undergo RRRTM have a greater risk of losing ejaculation ability as a complication associated with this surgical intervention itself. Also they have a significantly higher frequency of reduced sexual activity and dissatisfaction with sex life, but only when compared with the surveillance group.

DISCUSSION

The number of men who experience sexual problems in connection with treatment for testicular cancer varies considerably. About one third of men tend to experience one or more sexual problems as of reduced sexual desire, orgasmic dysfunction, EJD, reduced sexual activity, dissatisfaction with sex life and/or ED.

Compared with healthy controls, testicular cancer patients as a whole, regardless of what treatment they receive, have significantly increased risk of ED, EJD and orgasmic dysfunction.

Dissection of lymph nodes or resection of residual retroperitoneal tumor mass are the only treatments shown to be able to cause a specific and persistent sexual dysfunction – namely loss of ejaculation ability (retrograde ejaculation).

During radiation therapy, ED and problems with orgasm and desire are seen in particular. During chemotherapy a global effect on sexuality is described, which appears to be temporary. During surveillance, reduced sexual desire and orgasmic dysfunction are seen in particular.

No long-term effect is observed, associated in particular with either surveillance or chemotherapy or radiation therapy. Therefore it can be suggested that sexual dysfunctions in patients with testicular cancer patients can be explained both as organic and psychosexual sequelae.

Several studies provide evidence that an essential psychosexual component is involved. Compared with the general population and patients with Hodgkin's lymphoma, testicular cancer patients experience a higher degree of anxiety symptoms and negative body image [21-23]. The anxiety symptoms are independent of the treatment modality, but have been found to be associated with having sexual problems and having peripheral neuropathy [23]. It is thus suggested that it is not only the fact of getting cancer that appears to cause a mental strain, but also the fact that the cancer involves the genitalia.

There are several organic side effects to the treatments for testicular cancer. These side effects can be, directly or indirectly, a contributory cause of sexual dysfunctions. As mentioned in the preceding section, chemotherapy for example can cause Raynaud's phenomenon and therefore increase the tendency for erectile dysfunction [20]. Similarly, the more acute side effects such as nausea, vomiting, electrolyte imbalance, thrombocytopenia and leukopenia [1] can cause increased malaise and fatigue and thus affect sexual interest, desire and activity. Where hormonal function is generally preserved in the remaining gonad [1], it may quite possibly be affected subsequently as a result of post-chemotherapy dysfunction in the Leydig cells [20]. It is known that reduced plasma testosterone in men (<6 mol/l) can have a negative effect on sexual desire, sexual interest and spontaneous nocturnal erection [20]. It should be emphasized, however, that there is a considerable variation in the relationship between plasma testosterone level and sexual dysfunctions, and among other things, no effect has been found on erection ability during visual erotic stimulation [24].

In general, the quality of the studies in this field is subject to considerable variation in methodological strength. As is evident from this review, there is wide variation in follow-up time, so it is unclear whether you are studying long-term or short-term effects. Furthermore, it appears that the more subjective dysfunctions (sexual desire, orgasmic sensation and sexual activity) are assessed to a greater extent as worsened, when reported retrospectively rather than prospectively, whereas the more objective dysfunctions such as ED and EJD are assessed to a greater extent as worsened when reported prospectively. Blackmore shows, in his study of 32 men, that those who underwent orchiectomy because of cancer reported better preoperative sexual function than men who underwent orchiectomy for benign reasons, and healthy controls. The author suggests that this phenomenon may be due to the fact that cancer patients have a built-in expectation of reduction in sexuality as a result of the cancer and thus have a tendency to overestimate their premorbid sexual capacity [25].

Standardized questionnaires are only rarely used for measuring sexual dysfunctions, as well as it is not stated whether a sexual dysfunction is primary, or whether it is secondary to another sexual dysfunction. The latter is important as there is in general a high degree of internal correlation between sexual dysfunctions [26]. For example, a person who experiences reduced sexual desire in connection with diagnosis or orchiectomy might well also experience ED, reduced sexual activity or dissatisfaction with sex life. Or conversely, ED may lead to a reduced sexual desire.

Taking all these circumstances into account, it can be stated that patients who are treated for testicular cancer may experience various sexual dysfunctions, but they seem to be primarily of a psychosexual and temporary nature. There are, however, considerable limitations associated with the studies that characterize this field, and there is a lack of prospective studies, in which the individual treatments are clearly differentiated.

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Key points

- About a third of patients with testicular cancer experience, in connection with the treatment, one or more sexual dysfunctions in the form of: reduced sexual desire, erectile dysfunction, reduced enjoyment of orgasm, reduced sexual activity and ejaculatory problems.
- It is difficult to establish direct organic lesions as a cause of the sexual dysfunctions resulting from the individual treatment modalities, but larger studies are lacking/missing.
- There is much to indicate that psychosexual mechanisms are of great importance for the sexual dysfunctions which are experienced as a result of the treatment.
- Resection of residual tumor mass may cause loss of ejaculation ability, as a result of damage to nerve fibres.
- There is a lack of prospective studies of the individual treatment modalities.

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