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Self-reported cognitive problems in testicular cancer patients: Relation to neuropsychological performance, fatigue, and psychological distress☆

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Abstract

Objective: There is a concern about negative cognitive effects of systemic chemotherapy. We prospectively explored self-reported cognitive problems in testicular cancer patients (TCPs) treated with and without chemotherapy. **Methods:** One hundred and twenty-two TCPs were interviewed about concentration and memory problems shortly after orchidectomy but before any additional treatment (baseline), and then at a median of 1 year after end of treatment (follow-up). Symptoms of psychological distress, fatigue, and peripheral neurotoxicity were assessed by questionnaires, and patients also underwent neuropsychological testing. Self-reported cognitive problems were compared between three treatments groups: no chemotherapy, one cycle of chemotherapy, and multiple cycles of chemotherapy. Variables associated with an increase of self-reported cognitive problems from baseline to follow-up were explored. **Results:** Significantly larger proportions of TCPs in the two chemotherapy groups had an increase of self-reported cognitive problems from baseline to follow-up compared to the no-chemotherapy group. Increase of self-reported cognitive problems was significantly associated with psychological distress, fatigue, lower level of education, and Raynaud-like symptoms, but not with a decline in neuropsychological test performance. **Conclusion:** In this explorative study of TCPs, an increase of self-reported cognitive problems from baseline to 1-year follow-up was associated with chemotherapy and with symptoms of fatigue and psychological distress at follow-up, while no significant association was found with a decline in neuropsychological test performance.

Keywords: Chemotherapy; Fatigue; Prospective study; Psychological distress; Self-reported cognitive problems; Testicular cancer patients

Introduction

Cognitive problems such as concentration and memory problems are frequently reported by cancer patients [1–3]. This has led to an increasing scientific focus on cognitive function (CF) after cancer treatment. There is a concern that systemic chemotherapy may have a negative effect on CF in cancer patients, but this association is still not well documented [4–6]. Most studies in this field have explored CF in breast cancer patients, and the prevalence of self-reported cognitive problems is high in this group of cancer patients [7,8]. However, a low concordance between self-reported cognitive problems and reduced neuropsychological functioning has been observed repeatedly [6,9–11], and the relation between self-reported cognitive problems and chemotherapy is unclear. Self-reported cognitive problems, but not reduced neuropsychological test performance, have been found to be significantly associated with psychological distress and fatigue [6,10,12]. Regardless of etiology,

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cognitive problems may have negative consequences for patients' daily functioning and well-being. More systematic knowledge of self-reported CF in several groups of cancer patients of both sexes are needed [2,13].

Two studies have investigated self-reported CF in testicular cancer patients (TCPs). Fosså et al. [14] prospectively studied CF as a dimension of quality of life in 666 TCPs treated with cisplatin-based chemotherapy. They found that 19% of the patients reported worsening of CF 2 years after chemotherapy compared to the pretreatment level; however, comparison with TCPs not treated with chemotherapy was unavailable. In a cross-sectional study of 182 TCPs assessed at a median of 3 years after end of treatment, Schagen et al. [15] observed that approximately one-third of the TCPs in all treatment groups [chemotherapy, radiotherapy, and surveillance (no additional treatment after surgery)] reported some cognitive problems. As for breast cancer patients, self-reported cognitive problems were associated with psychological distress and fatigue, but not with reduced neuropsychological test performance.

As part of a Norwegian study of CF in TCPs, we prospectively explored self-reported cognitive problems in patients treated with and without chemotherapy. Evaluations were performed after orchidectomy (surgical removing of the affected testicle) but prior to any additional treatment (baseline), and then at 1 year after end of treatment (follow-up). To our knowledge, this is the first prospective study of self-reported CF in TCPs, and the aims of the study were (1) to compare the proportions of TCPs with an increase of self-reported cognitive problems from baseline to 1-year follow-up among patients treated with different treatment modalities (no chemotherapy, one cycle of chemotherapy, or multiple cycles of chemotherapy) and (2) to study variables associated with an increase of self-reported cognitive problems from baseline to 1-year follow-up. Based on previous research, we hypothesized that (1) a larger proportion of TCPs treated with multiple cycles of chemotherapy have an increase of self-reported cognitive problems from baseline to 1-year follow-up compared with TCPs treated with no or with one cycle of chemotherapy; (2) an increase of self-reported cognitive problems from baseline to 1-year follow-up is significantly associated with psychological distress and fatigue at follow-up, but not with a decline in neuropsychological test performance.

Methods

Patients and procedures

Between August 2006 and September 2008, recently orchidectomized TCPs aged 18–60 were invited to participate in the present prospective study. Exclusion criteria were (1) severe mental disorders like psychoses or substance dependence disorders; (2) degenerative brain disease or previous severe brain trauma; (3) brain metastases or severe somatic dysfunction; or (4) lacking proficiency in Norwegian language.

Evaluations consisted of a semistructured interview with predefined questions on concentration and memory function and on several background variables, some questionnaires, and a neuropsychological assessment. The complete neuropsychological results have been presented in a separate article [16]. Baseline evaluations were done after orchidectomy prior to start of any additional treatment, and follow-up evaluations were scheduled approximately 12 months after end of chemotherapy/start of surveillance period. All evaluations were performed by the first author and the order of the assessments at evaluations was as follows: (1) semistructured interview, (2) neuropsychological testing, and (3) collection of questionnaires filled in by the patients before the evaluation.

Information about stage of testicular cancer (TC) [17] and of treatment received was obtained from the medical records. Treatment of TC after orchidectomy is decided based on stage of disease, histology, and biochemical markers. In general, localized disease (Stage I) is treated with no or with one cycle of chemotherapy, while metastatic disease (Stage II–IV) is treated with two or more cycles of chemotherapy [18].

Among 202 eligible TCPs, 129 (64%) patients were recruited at baseline. Attrition analyses showed no significant differences between included and nonincluded patients concerning age or stage of TC. From 129 patients examined at baseline, 122 tumor-free TCPs (95% follow-up rate) were reevaluated at follow-up at a median of 12 months (range 8–23 months) after end of chemotherapy/start of surveillance. Seven patients were lost to follow-up: three denied reevaluation, one had moved abroad, and three had developed severe somatic disease or psychiatric disorder.

Among the 122 TCPs reevaluated at follow-up, 31 TCPs had received no chemotherapy (inclusive of one patient with radiotherapy only; NO-CHEMO group), 38 TCPs had received one cycle of chemotherapy (ONE-CHEMO group), and 53 TCPs had received two or more cycles of chemotherapy (MULTIPLE-CHEMO group). The chemotherapy regimens consisted of one treatment with carboplatin or of cycle(s) with bleomycin, etoposide, and cisplatin (BEP chemotherapy).

Data collection

Self-reported cognitive problems

In semistructured interviews at baseline and follow-up evaluation, the TCPs were asked the following two questions: *Baseline*: "In general, how is your concentration?"/"In general, how is your memory function?"; *Follow-up*: "How is your concentration?"/"How is your memory function?" The response alternatives were "very good," "good," "not so good," or "poor."

Only few patients at baseline and follow-up indicated that their concentration or memory function was "not so good" or