General Hospital Psychiatry 38 (2016) 21–25

Contents lists available at ScienceDirect

General Hospital Psychiatry

journal homepage: http://www.ghpjournal.com

Anxiety and depression in long-term testicular germ cell tumor survivors☆

S. Vehling, Ph.D. [a,*], A. Mehnert, Ph.D. [a,b], M. Hartmann, M.D. [c], C. Oing, M.D. [d], C. Bokemeyer, M.D. [d], K. Oechsle, M.D. [d]

[a] Department of Medical Psychology, University Medical Center Hamburg, Eppendorf, Hamburg, Germany
[b] Department of Medical Psychology and Medical Sociology, Division of Psychosocial Oncology, University Medical Center Leipzig, Germany
[c] Department of Urology, University Medical Center Hamburg, Eppendorf, Hamburg, Germany
[d] Department of Oncology, Hematology and Bone Marrow Transplantation with section of Pneumology, University Medical Center Hamburg, Eppendorf, Hamburg, Germany

ARTICLE INFO

Article history:
Received 8 June 2015
Revised 28 August 2015
Accepted 1 September 2015

Keywords:
Testicular cancer
Survivorship
Anxiety
Depression
Psychological distress

ABSTRACT

Objective: Despite a good prognosis, the typically young age at diagnosis and physical sequelae may cause psychological distress in germ cell tumor survivors. We aimed to determine the frequency of anxiety and depression and analyze the impact of demographic and disease-related factors.
Method: We enrolled *N*= 164 testicular germ cell tumor survivors receiving routine follow-up care at the University Cancer Center Hamburg and a specialized private practice (mean, 11.6 years after diagnosis). Patients completed the Generalized Anxiety Disorder Screener-7, the Patient Health Questionnaire-9 and the Memorial Symptom Assessment Scale-Short Form.
Results: We found clinically significant anxiety present in 6.1% and depression present in 7.9% of survivors. A higher number of physical symptoms and having children were significantly associated with higher levels of both anxiety and depression in multivariate regression analyses controlling for age at diagnosis, cohabitation, socioeconomic status, time since diagnosis, metastatic disease and relapse. Younger age at diagnosis and shorter time since diagnosis were significantly associated with higher anxiety.
Conclusion: Although rates of clinically relevant anxiety and depression were comparably low, attention toward persisting physical symptoms and psychosocial needs related to a young age at diagnosis and having children will contribute to address potential long-term psychological distress in germ cell tumor survivors.

1. Introduction

Male germ cell tumor is a highly curable malignant disease with an overall survival rate of 95%. Up to 80% of patients with metastatic disease achieve long-term survival after cisplatin-based combination chemotherapy plus secondary surgery or radiotherapy of residual tumor masses. At relapse, about 50% of patients survive after salvage multimodal treatment [1,2].

However, the typically young age at diagnosis between 15 and 40 years may increase the vulnerability for long-term psychosocial distress [3]. In addition, long-term physical sequelae of cancer treatment may interfere with the ability to maintain psychological well-being and give rise to increased levels of psychological distress [4,5].

Previous studies have reported clinically significant anxiety in 17–19% of long-term germ cell tumor survivors; these rates were significantly higher than in the age-matched normal population [6–8]. In early periods of survivorship up to 5 years after diagnosis, other studies have found anxiety rates of 19% [9], 28% [10] and 24% [11]. However, the frequency of clinically significant depression in earlier studies was comparable to normal population rates ranging between 8 and 10% [6–8]. While Rossen et al. [12], Eberhard et al. [9] and Bumbasirevic et al. [13] reported somewhat lower frequencies between 2 and 6%, higher rates of depression (15–17%) have yet been documented more often in the first years after treatment [10,14–16].

Previous prevalence data are, however, compromised by their almost exclusive reliance on the Hospital Anxiety and Depression Scale, as recent reviews have reported its poor ability to detect cases of clinically significant anxiety and depression [17,18]. In addition, only few studies have conducted controlled multivariate analyses of demographic and disease-related predictors of anxiety and depression in long-term survivors of germ cell tumor. Dahl et al. [7] found higher anxiety related to younger age, peripheral neuropathy and sexual problems, controlling for education, employment status, time since treatment, treatment type and relapse. Rossen et al. [12] found higher depression in patients living alone, controlling for age, time since diagnosis, relapse and treatment type.

The present study aimed to (a) determine the frequency of anxiety and depression in long-term germ cell tumor survivors as assessed by the Generalized Anxiety Disorder Screener-7 (GAD-7) and the Patient

☆ Conflicts of interest: None.

* Corresponding author at: Department of Medical Psychology, University Medical Center Hamburg, Eppendorf, Martinistr. 52 – W26, 0246 Hamburg, Germany. Tel.: +49-40-7410-56805; fax: +49-40-7410-4940.
E-mail address: s.vehling@uke.de (S. Vehling).

http://dx.doi.org/10.1016/j.genhosppsych.2015.09.001
0163-8343/

Health Questionnaire-9 (PHQ-9) and (b) to analyze the impact of demographic and disease-related factors on anxiety and depression within a controlled multivariate model. We hypothesized that higher levels of anxiety and depression would be related to younger age at diagnosis, shorter time since diagnosis and a higher number of physical symptoms, controlling for the following potentially confounding variables: cohabitation, having children, socioeconomic status, metastatic disease at first diagnosis and cancer relapse. This study is part of a larger survey including detailed assessment of physical symptom burden, quality of life, meaning in life and existential distress, for which results will be reported separately.

2. Materials and methods

2.1. Procedures

In this cross-sectional study, we enrolled all adult male germ cell tumor survivors receiving routine follow-up care at the uro-oncological outpatient ward of the University Medical Center within the University Cancer Center Hamburg and a specialized private practice in Hamburg, Germany, in October 2012. Eligible patients had completed antitumor treatment for at least 12 months prior without any further evidence of disease. Exclusion criteria were severe cognitive and physical impairment and insufficient proficiency in German to complete questionnaires and provide written informed consent. All patients who fulfilled the study inclusion criteria were contacted by their treating germ cell tumor specialist either in a personal conversation or via mail and were asked to complete a set of questionnaires. Patients provided written informed consent prior to study inclusion. The study received ethical approval by the ethics committee of the Medical Council in Hamburg, Germany.

2.2. Measures

We obtained sociodemographic data by use of a standardized self-report questionnaire. Disease-related characteristics were retrieved from medical records. We used the following validated self-report questionnaires:

The GAD-7 [19,20] measures the frequency of symptoms of generalized anxiety disorder during the past two weeks according to DSM-IV (Diagnostic and Statistical Manual of Mental Disorders - IV) criteria on a scale from 0 (*not at all*) to 3 (*nearly every day*). GAD-7 scores range from 0 to 21. Scores ≥10 indicate moderate anxiety and scores ≥15 indicate severe anxiety.

The PHQ-9 [21] measures the frequency of major depression symptoms during the past two weeks according to DSM-IV criteria on a scale from 0 (*not at all*) to 3 (*nearly every day*). PHQ-9 scores range from 0 to 27. Scores ≥10 indicate moderate depression and scores ≥15 indicate severe depression.

The Memorial Symptom Assessment Scale – Short Form [22] measures the presence of 28 physical symptoms common in cancer patients during the past week.

We calculated the multidimensional socioeconomic status index (SES) as an aggregate score of school and professional education level, occupational status and income. Calculation followed the standardized procedure applied by the German Health Survey [23,24]. SES scores range from 3 to 21. A low SES refers to scores ≤8, a middle SES to scores between 9 and 14 and a high SES refers to scores ≥15.

2.3. Statistical analysis

We calculated descriptive statistics including means, standard deviations and frequencies for dependent and predictor variables. Group differences and bivariate associations were calculated by ANOVA (analysis of variance, effect size: η^2), *t* tests (effect size: d), χ^2-tests (effect size: φ) and Pearson correlation coefficients. We conducted hierarchical multivariate regression analyses in order to analyze predictors of anxiety and depression. All regression analyses used forced entry method. We calculated two subsequent regression models: at first, a regression model including demographic predictors only was calculated (Model I). In Model II, disease-related predictors were added to the regression model in order to control for potential suppressor effects between demographic and disease-related predictors. Dichotomous predictors were dummy-coded, and continuous predictors as well as dependent variables were standardized prior to regression analyses. Unstandardized regression coefficients are reported only due to limited interpretability of standardized coefficients for dichotomous predictors. For continuous variables, unstandardized regression coefficients are, however, equal to standardized coefficients due to prestandardization of continuous variables. Multicollinearity among predictors was assessed by their intercorrelations and variance inflation factors. Inspection of regression residuals showed no evidence of nonlinear associations between predictors and dependent variables, heteroscedasticity of residuals or extreme outliers.

Missing values occurred in 12 cases for income, 2 cases for number of physical symptoms and 1 case for anxiety and depression. We imputed missing values by predictive mean matching using the R package MICE [25]. Predictors of the imputation model were all predictors specified for the regression model as well as education, occupational situation, number of chemotherapy cycles, type of surgery and radiotherapy. All *P*-values are two sided. We conducted analyses with R Version 3.1.3 and PASW (Predictive Analytics SoftWare) version 18.0.

3. Results

3.1. Sample characteristics and frequency of anxiety and depression

Of the 255 eligible patients approached, 61.1% (N=164) completed the questionnaire. Participants and nonparticipants did not differ in terms of age (d=0.24, $P=0.18$), years since diagnosis (d=0.16, $P=0.39$) and presence of metastases at first diagnosis ($\varphi=0.00$, $P=0.98$). Table 1 presents demographic and disease-related characteristics of the study sample. The mean time since diagnosis was M=11.6 years (S.D.=7.4). Most frequent physical symptoms were lack of energy (49%), feeling drowsy (42%) and sleeping problems (36%). Table 2 shows frequency and average levels of anxiety and depression. At least moderate anxiety occurred in 6% of the patients ($n=10$). At least moderate depression occurred in 8% of the patients ($n=13$).

3.2. Impact of demographic and disease-related variables on anxiety and depression

Table 3 reports bivariate correlations between predictor variables and anxiety and depression. Regarding remaining demographic and disease-related characteristics, no significant effects on anxiety and depression (d≤0.20 or $\eta^2 \leq 0.01$, $P \leq 0.13$) were found. There was no multicollinearity among predictor variables, as their intercorrelations were ≤0.40 (Table 3) and variance inflation factors were ≤1.4.

Table 4 shows results of multivariate regression analyses. In all models, predictors were entered simultaneously (forced entry method). Model I determined the impact of demographic variables on anxiety and depression. In Model II, disease-related variables were added. In both models, patients with children showed significantly higher levels of anxiety and depression. This effect increased when disease-related factors were controlled in the second model: having children was associated with an average increase of 0.4 standard deviations in both anxiety and depression levels compared to not having children [anxiety: b=0.43, 95% confidence interval (CI)=0.15 to 0.71, $P=0.003$, depression: b=0.37, 95% CI=0.11 to 0.62, $P=0.006$]. Moreover, a higher number of physical symptoms was significantly associated with higher anxiety and depression: a one-standard deviation increase in physical symptoms was associated with an average increase of 0.6 standard