

Perception of treatment burden, psychological distress, and fatigue in thyroid cancer patients and their partners – effects of gender, role, and time since diagnosis

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Abstract

Objectives: The aim of this study was to examine diagnosis and treatment burden as well as psychological distress (anxiety and depression) and fatigue in thyroid cancer patients and their partners, focusing on the effects of gender, role, and time since diagnosis.

Methods: Seventy-one patients diagnosed and treated for differentiated thyroid cancer within the past 7 years, participated in this online study, as well as 40 partners. Standardized questionnaires were used rating anxiety, depression, fatigue, and quality of life. Suffering in the context of diagnosis and treatment was evaluated using numeric analog scales. Patients' most recent hormone status was integrated into analysis.

Results: Male and female patients but not their partners had significantly higher mean anxiety scores ($p < 0.001$) than the norm. Severe fatigue that warrants observation and treatment was reported by two of 21 male patients (9.5%), 12 of 50 female patients (24%), two of 28 male partners (7.1%), and no female partners. With respect to diagnosis and treatment burden, female partners expressed the highest burden, while male patients expressed the lowest. This burden was associated with current fatigue levels in male patients and with current anxiety, depression, and fatigue levels in female patients.

Conclusions: Although both patients and partners suffer from the diagnosis and treatment of differentiated thyroid cancer, only patients are at risk of developing anxiety symptoms or fatigue. A simple question like 'How did being told you have thyroid cancer affect you?' might successfully screen for patients who are at risk.

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Introduction

Differentiated thyroid cancer (DTC) is the fifth most common tumor in women and in Europe, the second most common cancer in women below 45 years of age [1]. DTC represents about 90% of all thyroid cancer cases and generally has an excellent prognosis [2]. In a recent study involving the population-based profiles registry [3], thyroid cancer [4] survivors more often classified themselves as fatigued or very fatigued compared to the normative population [3]. Beside fatigues, anxiety rates are high in thyroid cancer survivors (37% with borderline and 26% definite anxiety) [5], as well as psychological distress (34.3%) [6], while depressive disorders are low (4.8%) [7]. Anxious-preoccupation and helpless–hopeless adjustment styles are associated with psychological distress [8]. From studies of other cancer sites, it has been shown that the prevalence of psychological distress among partners is approximately 20–30% [9], depending upon the type [10] and stage of disease [11]. To date, although there has been some understanding regarding the psychological effects of the diagnosis, treatment, and follow-up of thyroid cancer patients, there is limited understanding about these effects in partners.

The first aim of this retrospective cross-sectional multicenter study was to measure the perception of burden, among patients and their partners, immediately following the diagnosis and during the treatment of DTC. Perception of burden in this context was defined as the perception of psychological suffering in the context of the DTC diagnosis and treatment. We hypothesized first that patients, as well as partners, would be burdened by the diagnosis and treatment of thyroid cancer. Relative to the general population, even years after treatment, both will report higher incidences of self-reported anxiety, depression, and fatigue, as well as decreased quality of life (QoL). Our second hypothesis was that female patients would report higher mean scores for self-reported anxiety, depression, and fatigue, as well as lower mean levels of QoL than male patients, and, similarly for partners as women are generally more distressed than their male counterparts, regardless of their role as a patient or partner [12]. Our second aim, albeit limited to cross-sectional data, was to determine if differences exist with respect to self-reported anxiety, depression, and fatigue between short-term, medium-term, and long-term survivors. From our clinical experience and consistent with fatigue scores in the Eindhoven Cancer Profiles registry [3], we thirdly hypothesized that short-term survivors

and partners of short-term survivors would have similar incidence rates for psychological distress (anxiety and depression) and fatigue as middle-term and long-term survivors and their partners. Our fourth and final hypothesis was that an association would be identified between suffering scores related to diagnosis and treatment and currently reported levels of anxiety, depression, and fatigue, both among patients and partners.

Materials and methods

This study was approved by the Ethics Committee of the Cantons of Zurich and Luzern. According to the declaration of Helsinki, all participants provided their written informed consent prior to inclusion.

Participants

One hundred and fifty-one patients diagnosed and treated (by operation and radioactive iodine treatment) for DTC within the Department of Nuclear Medicine in either Zurich or Luzern over the past 7 years, and their partners, were asked to participate in this online study. Those couples who agreed to participate were sent two internet links, one for the patient and one for the partner, thereby enabling each person online access to participant information. Patients and partners who did not have access to the internet but were willing to participate in the study were sent paper versions of the questionnaires.

Inclusion criteria for patients were as follows: treated DTC within the past 7 years; willingness to provide information on thyroid hormone levels; sufficient knowledge of the German language; and age between 18 and 70 years. For partners, inclusion criteria also were sufficient knowledge of German language and an age between 18 and 70 years. Because we did not use specific tools to measure dementia, a confounder that influences a person's complex attention and memory [13], we excluded patients >70 years. At this age, it has been shown that the prevalence of dementia is rising [14].

A total of 151 patients were contacted by letter. One letter was sent back to us as address unknown, 23 had to be excluded because of their age (>70 years), and two insufficient German language. From the final 125 patients, 71 agreed to participate (56.8%). Of these, 62 were living in a close relationship (>6 months), and 40 partners agreed to participate (64.5%).

Measures

1. Standardized on-line questionnaires

The Beck Anxiety Inventory (BAI) [15] was used to assess anxiety. Total scores equal to or greater than 8 differ between patients with versus without anxiety in the German version [16].

The Beck Depression Inventory (BDI) [17] was used to assess depressive symptoms. A total score equal to or greater than 10 differs between patients with versus without depression. The German version of the BDI has been found to have good internal consistency and validity [18].

The Brief Fatigue Inventory (BFI) [19] was used to measure fatigue. This rapid screening questionnaire has correlated strongly with the Functional Assessment of Cancer Therapy: Fatigue [20]. On the BFI, patients were asked whether they had experienced unusual fatigue or tiredness over the past week and how fatigue interferes with six aspects of their daily lives. A total score between 1 and 3 indicates mild fatigue, scores between 4 to 7 moderate, and scores from 8–10 severe fatigue that warrants observation and treatment [21].

The World Health Organization Quality of Life questionnaire, [22], was used to measure subjective QoL in patients and their partners and generating scores on physical health, psychological health, social relationships, and environment. It also includes two items on global QoL [23].

The German version of the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire [24] was used to assess health-related QoL (HRQoL) in patients. The 30 items measure global health status, functional scales (physical, emotional, role, cognitive, and social functioning), symptom scales (fatigue, nausea/vomiting, and pain), and single symptom items (dyspnoea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties) [25], [26].

Medical and demographic variables: Questions about medical information included asking about any potential secondary cancer diagnoses and treatment; the duration of time since first diagnosis and treatments undergone since diagnosis; Participants also reported their age and gender, education level, household income, partnership duration, number of children, and living arrangement. Furthermore, we asked patients and their partners questions regarding the perception of burden in the context of the diagnosis and treatment, using numeric rating scales. For example, patients and partners were asked the following question: (a) How did being told you have thyroid cancer affect you? Subjects were asked to indicate a number between 0 and 10, where 0 meant 'not burdened' and 10 meant 'extremely burdened'. The questions for this rating scale were derived from our clinical experience working with thyroid cancer patients and were constructed analogous to the distress thermometer [27,28]. Further questions related to: (b) Their surgical resection: How did you experience the surgery?; (c) Fear of radioactive iodine (RAI): Did you have any fears about exposure to radioactivity? ("0" meant 'no, not at all' and "10" meant 'yes, very much'); (d) RIA: What was your experience with the radioiodine treatment?; (e) Isolation: How did you experience the isolation?; (f) Being radio-active:

Was the fact that you were still a little bit radioactive after the RAI treatment worrisome for you?; (g) Non-closeness: How much did you suffer from the lack of physical closeness to other people during and shortly after your RAI treatment?

2. Clinical assessment

Each patient's hormone status (FT3, FT4, thyroid-stimulating hormone (TSH), and thyroglobulin and anti-thyroglobulin antibodies) within the past year of his/her last routine clinical control either at the Departments of Nuclear Medicine in Zurich or in Luzern also was obtained and integrated into analysis.

Data analysis

Descriptive statistics were used to characterize the sample of patients and partners. To compare mean values with norm values or values from the literature, one-sample *t*-tests were applied. Paired sample *t*-tests were used to compare mean values between patients and their partners (role differences). To gain further insights into potential gender differences, independent sample *t*-tests were performed. Bivariate Pearson correlation coefficients were calculated to identify associations between patients' hormone status and core outcome variables (BAI, BDI, BFI, and QoL). The sample was further divided into three groups depending upon time since they were diagnosed with thyroid cancer: group 1: 7–12 months ($n=13$); group 2: 13–36 months ($n=27$); and group 3: 37–79 months ($n=31$). Differences in means between these three groups were identified using analysis of variance. To identify any correlations between the perception of burden secondary to the diagnosis or treatment of thyroid cancer and patients' current symptom scores (BAI, BDI, and BFI), a total suffering score was generated by summing all seven numeric analog scales pertaining to suffering in the context of diagnosis and treatment. All statistical calculations were performed using the software package IBM SPSS statistics (version 21.0, IBM, Armonk, NY, USA). The threshold for statistical significance was set at $p \leq 0.05$ (two-sided).

Results

Socio-demographic, medical, and hormone characteristics

Socio-demographic data are presented in Table 1. Ten patients (14.1%) had a history of a previous non-thyroid cancer (two breast, one skin, one lung, two colon, and four others). Three couples (4.2%) were separated over the course of the disease, a separation that they did not attribute to the disease.

Table 1. Socio-demographic characteristics of patients and their partners ($n = 71$ patients and 40 partners)

	Patients		Partners	
	<i>n</i>	%	<i>n</i>	%
Gender	–	–	–	–
Male	21	29.2	28	70
Female	50	69.4	12	30
Age (M (SD, range)) in years	47.31 (11.6 (24–70))	–	47.21 (11.7 (26–68))	–
Education	–	–	–	–
Obligatory school	7	9.7	1	1.4
Apprenticeship	32	44.4	16	22.2
High school	3	4.2	1	1.4
Technical college	12	16.7	13	18.1
University degree	11	15.3	8	11.1
Others	4	5.6	0	–
Missing	2	2.8	1	1.4
Employment	–	–	–	–
Full time	28	38.9	26	66.7
Part time	28	38.9	6	15.4
Unemployed	2	2.8	1	2.6
In training	1	1.4	0	–
Household	5	6.9	4	10.3
Retired	6	8.3	2	5.1
Missing	1	1.4	1	1.4
Partnership duration (M (SD, range)) in years	20.8 (13.4, 0.5–50)	–	–	–
Number of children	–	–	–	–
0	19	26.4	–	–
1	11	15.3	–	–
2	25	34.7	–	–
3	13	18.1	–	–
4	1	1.4	–	–
5	2	2.8	–	–
Living arrangement	–	–	–	–
With partner	56	82.4	–	–
With children	33	48.5	–	–
With parents	3	4.4	–	–
Alone	6	8.8	–	–
Apartment-sharing community	2	2.9	–	–
Time since the diagnosis (M (SD, range)) in months	37.6 (21.3, 7–79)	–	–	–
Radioiodine treatment	–	–	–	–
1	48	69	–	–
2	15	21	–	–
3	6	9	–	–
4	1	1	–	–

SD, standard deviation.

The current mean level of FT3 was 4.68 pmol/l (Standard deviation (SD) 1.26) (reference range: 3.6–6.4 pmol/l). Nineteen of 71 patients (26.8%) were under TSH suppression (TSH < 0.01 mU/l), which was clinically sought for high-risk thyroid cancer patients; meanwhile, 47 patients (66.2%) had higher TSH values. In five patients, current TSH hormone status was missing. Fifty-two of 71 patients (73.2%) had a thyroglobulin level < 0.9 µg/l (indicating tumor-free status), and 6/71 (8.5%) patients had a thyroglobulin level ≥ 0.9 µg/l; in 13 patients, current thyroglobulin status was missing. In 44 patients, we found antibodies against thyroglobulin (61.9%), while they were not detected in 21 (29.6%).

Anxiety, depression, fatigue, and quality of life

Relative to normative data from Germany (Swiss data were unavailable), male and female patients but not their partners had significantly higher mean anxiety scores ($p < 0.001$). A paired-sample t -test revealed a significant difference ($t = 2.649$, degrees of freedom (df) = 37, $p = 0.012$) between anxiety scores in patients and partners. Global fatigue scores were slightly higher in patients than in partners (not significant (ns)), although neither differed significantly from norm values. All other data are presented in Table 2. No gender differences were identified for any core variable, and there were no role differences (patient versus partner) for depression, fatigue, or QoL. Bivariate correlations between hormone status (FT3, FT4, and TSH) or numbers of radioactive iodine treatment and core outcome variables (BAI, BDI, BFI, and QoL) failed to detect any significance association. The distribution of anxiety, depression, and fatigue among patients and partners is summarized in Figure 1.

Influence time since diagnosis

To obtain further insights into whether or not the time since diagnosis might impact patients' or partners' current anxiety, depression, or fatigue level, the sample was divided into those three groups mentioned previously.

Mean levels of self-reported anxiety and depression did not differ significantly between these three groups, either among patients (anxiety ($F = 0.28$; $df = 2$; ns) and depression ($F = 0.25$; $df = 2$; ns)) or partners (anxiety ($F = 0.71$; $df = 2$; ns) and depression ($F = 1.52$; $df = 2$; ns)). Similar results were noted for fatigue, again for both patients (fatigue global score ($F = 1.47$; $df = 2$; ns), fatigue severity ($F = 1.39$; $df = 2$; ns), and fatigue interference ($F = 1.22$; $df = 2$; ns)) and partners (fatigue global score ($F = 3.15$; $df = 2$; ns), fatigue severity ($F = 2.44$; $df = 2$; ns), and fatigue interference ($F = 2.25$; $df = 2$; ns)).

Perceived burden of diagnosis and treatment

As demonstrated in Figure 2, female partners reported the highest levels of burden from diagnosis and treatment, while male patients suffered the least when informed about their thyroid cancer diagnosis or while being treated. To further analyze whether there was any association between the perceived burden from diagnosis and treatment and currently measured psychological distress (BAI and BDI) and fatigue, a total suffering score was constructed by adding the seven numeric rating-scale scores. The reliability (Cronbach's alpha) of this suffering scale was high both in patients (0.87) and in partners (0.76). The male patient and female partner summation scores differed ($t = -6.482$; $df = 11$; $p < 0.001$), but this

Table 2. Gender and role differences with respect to core variables ($n = 71$ patients and 40 partners)

Variable	Male M (SD)	Female M (SD)	All ^b M (SD)	t-test ^a t	df	p
BAI	–	–	–	–	–	–
Patient	5.9* (7.4)	7.8* (9.6)	7.2 (9.0)	–0.783	69	0.44
Partner	2.5 (3.8)	2.6 (3.0)	2.7 (3.8)	–0.585	37	0.56
Norm	2.4 (4.5)	3.8 (5.7)	–	–	–	–
BDI	–	–	–	–	–	–
Patient	4.5 (6.6)	6.3 (6.7)	5.8 (6.7)	–1.059	68	0.29
Partner	3.9 (6.3)	4.5 (4.6)*	4.2 (5.8)	–0.430	38	0.67
Norm	5.9 (9.6)	6.5 (9.4)	–	–	–	–
BFI (global)	–	–	–	–	–	–
Patient	2.1 (1.6)	2.8 (2.2)	2.6 (2.1)	–1.274	68	0.21
Partner	1.8 (1.8)	2.2 (1.0)	1.9 (1.6)	–0.818	38	0.42
Norm	–	–	2.2 (1.8)	–	–	–
WHOQoL-Bref (overall)	–	–	–	–	–	–
Patient	78.7 (17.7)	74 (20.2)	75.4 (19.5)*	0.920	68	0.36
Partner	78.1 (15.8)	75 (17.7)	77.2 (16.2)*	0.553	38	0.58
Norm	64.3 (18.3)	68.1 (17.2)	66.3 (17.7)	–	–	–
EORTC QLQ-C30 (overall)	–	–	–	–	–	–
Patient	80.8 (15.5)*	74 (20.4)*	75.9 (19.3)*	1.344	68	0.183
Norm	65.6 (23.4)	67.9 (29.9)	66.9 (23.7)	–	–	–
EORTC QLQ-C30 (fatigue)	–	–	–	–	–	–
Patient	18.33 (18.1)	24.0 (22.9)	22.4 (21.7)*	–0.987	68	0.327
Norm	–	–	30.1 (25.6)	–	–	–

SD, standard deviation; df, degrees of freedom; BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory; BFI, Brief Fatigue Inventory; WHOQoL-Bref, World Health Organization Quality of Life questionnaire; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire.

^at-test for gender difference.

^bNo significant role differences between patients and partners with exception of BAI ($t = 2.649$, $df = 37$, $p = 0.012$).

*Significant different from the norm $p < 0.05$ (one sample t-test).

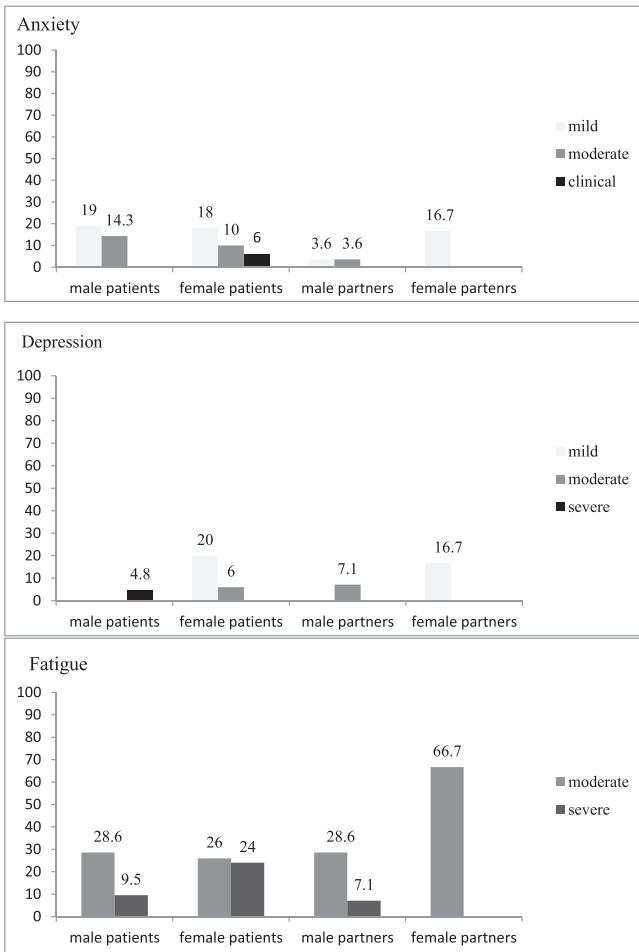


Figure 1. Distribution of anxiety, depression, and fatigue in 21 male patients, 50 female patients, 28 male partners, and 12 female partners in percent

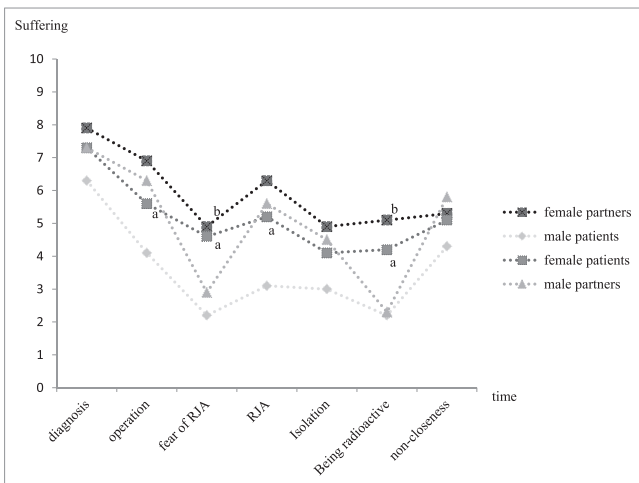


Figure 2. Perception of burden ($n=71$ patients and 40 partners). RJA, radioactive iodine treatment. ^a t -test for gender difference in patients ($p < 0.05$). ^b t -test for gender difference in partners ($p < 0.05$)

was not evident between female patients and their male partners ($t=0.783$; $df=26$; $p=0.441$). In male patients, the total suffering score was moderately correlated with global fatigue ($r=0.63$; $p < 0.01$), fatigue severity ($r=0.50$; $p < 0.05$), and fatigue interference ($r=0.62$; $p < 0.01$), but with neither anxiety nor depression. In female patients, the suffering score was moderately correlated with anxiety ($r=0.47$; $p < 0.01$), depression ($r=0.41$; $p < 0.01$), and interference ($r=0.40$; $p < 0.01$), and weakly correlated with global fatigue ($r=0.39$; $p < 0.01$) and fatigue severity ($r=0.31$; $p < 0.05$). No associations were discovered between total suffering and core outcome variables (anxiety, depression, and fatigue) in male or female partners.

Discussion

To our knowledge, this is the first study to examine treatment burden, psychological distress, and fatigue in thyroid cancer patients and their partners. Our results highlight that generally patients (males and females) and not their partners suffer from anxiety symptoms after being diagnosed and treated for DTC. This was unexpected, because partners, mainly females, reported the highest levels of burden relating to the patient’s diagnosis and treatment. Such suffering when thyroid cancer is initially diagnosed and treated is not associated with later psychological distress or fatigue in partners, although it is in patients. In this regard, early perception of burden was associated with fatigue in males, versus anxiety, depression, and fatigue in females.

Discussing our results in light of the current literature, we note that only patients and not partners reported elevated levels of anxiety, which is somewhat consistent with our first hypothesis and contrary to findings in patients with cancer at other anatomical sites [29]. Contrary to our expectations, mean depression and fatigue levels did not differ significantly from norm values, and overall QoL and some QoL sub-scores were actually higher than normative means. This is surprising and different than what has been published in the literature [30,31]. However, Husson *et al.* [3] found in their review of studies on HRQoL of thyroid cancer survivors that surgery had a negative impact on short-term HRQoL scores but that the scores returned to pre-operative levels when time since surgery increased. In our sample, the mean time since diagnosis was just 3.1 years, much shorter than Hoftijzer’s 6.5 years [31], although sub-analysis failed to detect any difference between those patients whose diagnosis was made within the past year and those diagnosed 1–3 years previously or even earlier.

About 20% of our patients reported suffering from severe fatigue, which is almost half the 35% rate identified by Mendoza *et al.* [19]. Mendozas’ group examined

inpatients as well as outpatients from several departments, including bone marrow transplantation, hematology, gastrointestinal oncology, and radiation oncology. There is evidence in the literature that the rates of fatigue vary depending on the patient population and type of treatment received [32], which might explain our lower rates. In partners, 5.1% claimed to be severely fatigued, which is in line with data from a community control population [19]. When comparing our results against others, one must keep in mind that many authors combine moderate and severe fatigue rates so that rates of fatigue of 30–60% during treatment are common. This rate tends to decline by the first year following treatment, although 25–30% of patients experience fatigue for years [33,34]. Combining moderate and severe fatigue rates, we found prevalence rates in our sample of 38.1% among male patients, 50% in female patients, 35.7% in male partners, and 66.7% in female partners. These rates are similar to those reported (52% of 174 patients) for a large sample of American thyroid cancer survivors.

A consistent gender effect, as previously reported by Hagedoorn *et al.* [12], was not evident in our sample, neither among patients nor in partners. Although descriptive analyses revealed a pattern supporting our second hypothesis, with higher mean scores for anxiety, depression, and fatigue in female patients relative to male patients and lower mean QoL scores in females, these differences were not statistically significant. Similar results were obtained with respect to partners.

With respect to our third hypothesis, seemingly short-term survivors and their partners had higher rates of anxiety, depression, and fatigue than middle-term and long-term survivors and their partners. However, mean anxiety, depression, and fatigue levels did not differ significantly between the three time-since-diagnosis groups, neither among patients nor partners. This is congruent with the results of a study involving the Eindhoven Cancer Profiles registry, in which the investigators identified a relatively stable rate of fatigue among short-term (<5 years) and different subsets of long-term (5–10, 10–15, and >15 years) survivors [3]. Last but not least, we were only able to partially confirm our last hypothesis, which might be of distinct interest to clinicians. In male patients, scores indicating level of

perceived burden related to the diagnosis and treatment of thyroid cancer were correlated with current fatigue scores. In female patients, such suffering scores were not only correlated with current fatigue scores but also with current levels of anxiety and depression. In partners, we failed to detect any such associations. Neither patients' hormone status nor the numbers of radioactive iodine treatment were associated with our outcome variables, which is in line with the literature [6,31].

This is the first study to examine the burdens associated with the diagnosis and treatment of thyroid cancer, for both patients and their partners. Some methodological limitations of this study merit comment. One shortcoming is the cross-sectional design and retrospective nature of both patient-reported and partner-reported diagnosis and treatment burden, which do not allow for causal interpretation of the results. Our analyses with respect to time are based on subjects assessed once at diverse time-points after diagnosis. The retrospective assessment of the burden of diagnosis and treatment might be influenced by the actual mood. Future studies examining these processes over time might provide a better understanding of how diagnosis and treatment burden and other variables influence anxiety, depression, fatigue, and QoL in thyroid cancer patients and their partners. Another potential sampling bias is that patients and partners who were not in good physical or psychological condition might have refused to participate in our study. This might be one reason for the unexpectedly low rate of depression we observed in our sample, relative to normative data, and the relatively high reported level of QoL.

Notwithstanding these limitations, it appears at least somewhat justified to derive the following clinical implications from our results. Patients, but not their partners, appear to be at increased risk of developing anxiety symptoms after being diagnosed and treated for DTC, even though both patients and partners are burdened in various ways at the time of diagnosis and treatment. A simple question like 'How did being told you have thyroid cancer affect you?' might lead to the early detection of patients who are potentially at risk of developing subsequent anxiety, depression, or fatigue and, hence, to more timely psychosocial referrals.

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