

THE MOST COMMON FACTORS INFLUENCING ON QUALITY OF LIFE OF THYROID CANCER PATIENTS AFTER THYROID HORMONE WITHDRAWAL

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SUMMARY

Background: The aim of study was to evaluate which factors impact mostly on life-quality of patients with differentiated thyroid carcinoma after thyroid hormone withdrawal.

Subjects and methods: 150 patients were enrolled in the study by using Quality of life- Thyroid version questionnaire in which they expressed their physical, psychological, social and spiritual well-being. The answers have been interpreted on a scale from 0 to 10. All patients underwent four weeks levothyroxine withdrawal in preparation for I-131 procedures and thyroglobulin testing.

Results: Individual statements on the physical subscale showed that patients had most difficulties with fatigue, intolerance to cold and heat, sleep changes and weight gain, but with higher average values than expected. Fatigue was one of the most common physical difficulties. Female patients had significantly more difficulties than male respondents. Five most expressed psychological difficulties have been stress caused by initial diagnosis, followed by stress caused by surgical treatment, fear of metastases, stress caused by initial radioiodine ablation treatment and fear of cancer recurrence. Generally, results revealed troubles mostly in physical symptoms relating to thyroid hormone withdrawal, as well as psychological distress caused by initial diagnosis. Respondents with higher educational level achieved a significantly higher score than less educated patients ($p=0.026$, Mann-Whitney U test). Illness was very distressing for their families (median value 1, range: 0 to 10) and they reported insufficient support from others (1, range: 0 to 10), but they did not feel isolated. Family and work consequences were less apparent.

Conclusion: The results of QOL-Thyroid questionnaire help to identify high-risk areas in patients' lives that are negatively affected by hormone withdrawal. Regarding the wide definition of quality of life, a positive impact on patients' recovery could be achieved by directing attention to most expressed difficulties noted in this questionnaire.

Key words: quality of life - differentiated thyroid carcinoma - thyroid hormone withdrawal - questionnaire

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INTRODUCTION

Increase of thyroid carcinoma incidence and favorable prognosis after treatment raised attention on quality of life (QOL) as an important part of patients' recovery (Dean & Hay 2000). Differentiated thyroid carcinomas (DTC) originate from follicular thyroid cells, and include papillary and follicular carcinoma and their variants. Their proportion is in majority, in the range of 70 to 90% (Mc Dougall & Berry 2006). Generally, patients with these types of carcinomas have a large survival rate of about 91% for the entire DTC group, although male patients, patients older than 45 years with unfavorable histology and larger tumor with extracapsular spread or distant metastases have a poorer prognosis (Almeida et al. 2009, Fahey et al. 1995, Pacini et al. 2010). Better screening methods are probably the reason for higher incidence of thyroid cancer, especially micropapillary carcinoma. Improved diagnostic procedures such as neck ultrasound followed by fine-needle aspiration biopsy of suspicious lesions make the possibility of early detection of thyroid malignancy as well as neck lymph node metastases (Nix et al. 2005). After initial diagnosis patients undergo total thyroidectomy usually followed by radioiodine ablation of remnant tissue.

Those initial treatment decreases the risk of recurrence by therapeutic effect on possible micrometastases, increases the sensitivity of serum thyroglobulin testing because the thyroid remnant tissue is a potential source of thyroglobulin and increases the sensitivity of further whole-body scanning as it removes residual functioning thyroid tissue (Pacini et al. 2010, Nix et al. 2005). Thyroid stimulating hormone (TSH) suppression after initial treatment is performed with levothyroxine to avoid pituitary gland to produce TSH which stimulates thyroid follicular cells, and, in that way, suppress the growth of any remaining thyroid cells (Nix et al. 2005). But, patients are periodically monitored for thyroid cancer recurrence with blood tests thyroglobulin measurement, I-131 whole body scan and neck ultrasound. As the sufficient TSH level (more than 30 mU/L) has an important role in radioiodine uptake and thyroglobulin secretion, patients should undergo four weeks L- thyroxine withdrawal in order to increase the successfulness of radioiodine ablation as well as sensitivity in searching for metastases. Those TSH production after thyroid hormone withdrawal leads to hypothyroid state that is associated with the serious side effects on physical, psychological and social aspects which can have a negative impact on the patient's quality of life

(QOL) (Wang et al. 2010). The one way to avoid these difficulties is application of recombinant TSH (rhTSH) that is justified, especially in older patients with chronic diseases, in patients who cannot achieve sufficient level of serum TSH and in ablation of remnants in low risk patients (Wang et al. 2010), but because of relatively high price its use is limited and sometimes not under reimbursement policy of health insurance.

The aim of this study was to measure QOL in DTC patients who undergo LT4 withdrawal due to clinical follow-up or in recently operated patients before radioiodine ablation. The study was made to identify which factors impact mostly on QOL in order to pay attention to noted signs with a purpose of improving patients' recovery.

SUBJECTS AND METHODS

Study Sample

The study included all thyroid cancer patients submitted for diagnostic or therapeutic radioiodine administration under thyroid hormone withdrawal to Clinical Department of Nuclear Medicine from September 2010 to April 2011. Out of 162 eligible patients, 158 (97.5%) agreed to participate in the study. Data from 8 of 158 participants (5%) had to be discarded because of incomplete responses. Thus, 150 patients were enrolled in the study (response rate 92.5 %). All patients underwent four weeks levothyroxine withdrawal before entering the study. 125 patients (83.3%) were in a periodical follow-up and 25 (16.7%) were recently surgically treated. Patients which have been submitted to hospital because of follow up received 185 MBq (5mCi) of I-131 as a diagnostic dose, while recently surgically treated patients received from 888MBq (24 mCi) to 3700 MBq (100 mCi) for thyroid remnant ablation. All applied procedures are part of routine diagnostic and therapeutic protocols that have been approved by the authorities. The study was approved by the institutional ethic committee and each patient signed an informed consent.

Questionnaire

Research is performed by using Quality of life - Thyroid version (QOLTV) questionnaire, which has been developed and recommended for future use by the City of Hope National medical center and Beckman Research Institute (Duarte, California, United States), which is the part of the United States National Cancer Institute especially designed to measure quality of life of differentiated thyroid carcinoma patients (Ferrell et al. 1995). The thyroid version was adapted from a form created for use in the general population of cancer survivors. The questionnaire consists of 56 statements divided into four subscales related to physical (PHWB), psychological (PSYWB), social (SOCWB) and spiritual well being (SPWB). The answers are numbered on a

scale from 0 to 10 with word anchors at each end of the scale. The answers are interpreted in a way that 0 means the worst outcome, and 10 mean the best outcome. Some answers have reverse order, so during the evaluation of results we had to switch the result by subtraction from number 10. We analyzed the statements individually and also as a composite score of physical, psychological, social and spiritual well-being. The questionnaire demonstrated good internal consistency; Cronbach α of the overall scale was 0.92. Subscale alphas ranged from 0.58 for spiritual well being, 0.82 for physical, 0.84 for social and 0.90 for psychological well being. The original English version of the questionnaire was translated into Croatian language to facilitate understanding of the questions for our patients. The patients completed the questionnaire after detailed explanation how to fulfill it and were given sufficient time to resolve dilemmas about the questionnaire. The patient was asked to read each question and then circle a number on a scale between 0 and 10 to show a level of agreement or disagreement with the statement during the period of hypothyroidism, with special emphasis on the last week of thyroxine withdrawal.

The questionnaire was completely anonymous. Patients had designation code in order to statistically process their data.

Demographic data included age, sex and education level.

Serum TSH concentration was determined at the time of completion of the questionnaire and all patients were hypothyroid with TSH values greater than 30 mIU/L (normal range 0.4-4.2 mIU/L). According to TSH level patients were divided into 3 groups: TSH level between 30 to 60 mIU/L (34 patients), 61-100 mIU/L (71 patients), and >100 mIU/L (53 patients).

According to education level patients were divided into two groups. First group included respondents with secondary education, and second group included tertiary (undergraduate and postgraduate) educated respondents.

Statistics

Cronbach's α was used as a measure of internal consistency, based on the average inter-item correlation for all questions and for statements related to physical, psychological, social and spiritual well being. Pearson's chi-square exact test, Mann-Whitney U-test or Kruskal-Wallis rank test, or simple linear regression were used for different comparisons in our bivariate analysis. All reported tests are two-sided.

Multivariate analysis was done by multiple linear regression for the physical, psychological, social and spiritual well being score as dependent variables respectively. Initially variables with a $p < 0.25$ on bivariate analysis were included in the model. There were no serious violations of the assumptions of linearity, normality of residuals, homoscedasticity and

no evidence of collinearity in our multivariate linear regression model. The statistical analysis was performed by STATA/IC ver.11.1. (StataCorp. 2009. Stata Statistical Software: Release 11. College Station, TX: StataCorp LP). Results of two-sided statistical tests in which P values were less than 0.05 were considered to be statistically significant.

RESULTS

A total of 150 patients (24.0 % male) were included in the study (response rate 92.5 %). The median age was 53 (range: 18 to 87) years. There was no statistically significant difference between sex regarding age ($p=0.30$, Kruskal-Wallis, d.f. 2). The socio-demographic data, clinical features and self-reported data are detailed in Table 1.

The median physical well being score was 78 (range: 26 to 127) out of maximum 130 points. Male respondents achieved a significantly higher score than female patients (median: 89, range 40 to 124 vs. 72.5, range 26 to 127; $p=0.005$, Mann-Whitney U test) (Table 2). There were no statistically significant differences in PHWB score between groups with different TSH level, educational level, between patients in follow-up and nearly operated patients, and regarding age. Mean TSH value \pm SD in the group was 82.5 ± 37.6 mIU/L (normal range 0.4-4.2 mIU/L).

The analysis of patients' individual statements on the PHWB subscale (Table 3) showed that they had most difficulties with fatigue (4, range: 0 to 10), intolerance to cold and heat (5, range: 0 to 10), sleep changes (5, range: 0 to 10) and weight gain (5, range: 0 to 10) (Table 2). Female patients had significantly more difficulties than male respondents with the following symptoms: fatigue (4, range: 0 to 10 vs 6, range 0 to 10;

$p=0.033$, Mann-Whitney U test), appetite changes (7, range: 0 to 10 vs 9, range 2 to 10; $p=0.034$, Mann-Whitney U test), sleep changes (5, range: 0 to 10 vs 6, range 1 to 10; $p=0.039$, Mann-Whitney U test), dry skin or hair changes (4, range: 0 to 10 vs 9, range 2 to 10; $p<0.001$, Mann-Whitney U test), voice changes (6, range: 0 to 10 vs 9.5, range 3 to 10; $p<0.001$, Mann-Whitney U test), swelling/ fluid retention (5, range: 0 to 10 vs 9, range 1 to 10; $p<0.001$, Mann-Whitney U test), but less with tolerance to cold and heat (6, range: 0 to 10 vs 3.5, range 1 to 10; $p=0.032$, Mann-Whitney U test).

Table 1. Demographic, clinical features and self-reported data

	Number (%)	Median (range)
Age (year)		53 (18-87)
Gender		
Male	36 (24)	
Female	114 (76)	
Educational level		
Secondary education	112 (74.7)	
Tertiary	38 (25.3)	
Follow-up	125 (83.3)	
Ablation	25 (16.7)	
TSH (mIU/L)		
30 to 60	33 (22)	
61-100	66 (44)	
>100	51 (34)	
QOLTV*		
Physical WB** (0-130)		78 (26-127)
Psychological WB (0-220)		107 (41-199)
Social WB (0-140)		78.5 (20-129)
Spiritual WB (0-70)		38 (10-70)

*QOLTV - Quality of life - Thyroid version; **WB - well being

Table 2. Comparison of thyroid patients well being by age, gender, way of radioiodine application, education and TSH level

Variables	No. of patients	Physical well being		Psychological well being		Social well being		Spiritual well being	
		Median (range)	P	Median (range)	P	Median (range)	P	Median (range)	P
Age*									
<40	27	77 (43-122)	0.45	114 (53-199)	0.36	89 (50-129)	0.23	41 (10-70)	0.49
40-60	81	79 (26-124)		102 (41-199)		77 (21-125)		39 (13-64)	
>60	42	70 (33-127)		111 (54-199)		76 (20-120)		37 (14-65)	
Gender†									
Male	36	89 (40-124)		119 (59-199)		82.5 (43-129)		35 (13-60)	
Female	114	72.5 (26-127)	0.005	103.5 (41-199)	0.06	77 (20-125)	0.10	39.5 (10-70)	0.41
Follow-up†	125	78 (26-127)		107 (41-199)		80 (21-129)		39 (10-70)	
Radioablation†	25	79 (33-124)	0.52	106 (71-197)	0.77	73 (20-120)	0.25	36 (18-65)	0.62
Educational level†									
Secondary	112	76 (26-127)		105 (41-199)		78 (20-125)		38 (13-65)	0.54
Tertiary	38	83 (41-122)	0.12	113 (51-199)	0.11	81.5 (21-129)	0.026	40 (10-70)	
TSH (mIU/L)*									
30 to 60	33	71 (26-122)	0.28	106 (49-199)	0.71	81 (35-123)	0.72	41 (21-70)	0.12
61-100	66	77 (32-124)		102.5 (41-197)		75 (20-125)		36 (10-65)	
>100	51	80 (40-127)		112 (51-199)		82 (21-129)		40 (13-60)	

*Comparison of patients well being score; Kruskal-Wallis rank test; †Comparison of patients well being score; Mann-Whitney U-test

Table 3. Physical, psychological, social and spiritual symptoms tests during levothyroxine withdrawal in patients with thyroid carcinoma by sex

Statement	All patients (n=150) Median (range)	Male (n=36) Median (range)	Female (n=114) Median (range)	P value*
Physical well being	78 (26-127)	89 (40-124)	72.5 (26-127)	0.005
Fatigue	4 (0-10)	6 (0-10)	4 (0-10)	0.033
Appetite changes	7 (0-10)	9 (2-10)	7 (0-10)	0.034
Aches or pain	9 (0-10)	9 (1-10)	8 (0-10)	NS
Sleep changes	5 (0-10)	6 (1-10)	5 (0-10)	0.039
Constipation	10 (0-10)	10 (1-10)	9 (0-10)	NS
Menstrual changes or fertility	10 (0-10)		10 (0-10)	NS
Weight gain	5 (0-10)	7 (0-10)	5 (0-10)	NS
Tolerance to cold and heat	5 (0-10)	3.5 (0-10)	6 (0-10)	0.032
Dry skin or hair changes	6 (0-10)	9 (2-10)	4 (0-10)	<0.001
Voice changes	7 (0-10)	9.5 (3-10)	6 (0-10)	<0.001
Motor skills/ coordination	6 (0-10)	8 (1-10)	6 (0-10)	NS
Swelling/ fluid retention	6 (0-10)	9 (1-10)	5 (0-10)	<0.001
Overall physical health	5 (0-10)	6 (1-10)	5 (0-10)	NS
Psychological well being	107 (41-199)	119 (59-199)	103.5 (41-199)	NS
Difficulties coping with disease and treatment	6 (0-10)	7 (2-10)	6 (0-10)	NS
Quality of life	6 (0-10)	6.5 (0-10)	6 (1-10)	NS
Happiness	6.5 (0-10)	7 (1-10)	6 (0-10)	NS
Feel of control of things in life	7 (0-10)	7 (0-10)	7 (0-10)	NS
Satisfaction in life	7 (0-10)	7 (0-10)	7 (0-10)	NS
Ability to concentrate and remember things	5 (0-10)	4 (0-10)	5 (0-10)	NS
Feeling useful	7 (0-10)	7 (0-10)	7 (0-10)	NS
Changes in patient's appearance	5 (0-10)	7 (0-10)	5 (0-10)	NS
Changes in self- concept	6 (0-10)	6 (0-10)	6 (0-10)	NS
Distress caused by: initial diagnosis	2 (0-10)	2 (0-10)	2 (0-10)	NS
surgery	3 (0-10)	3 (0-10)	3 (0-10)	NS
whole treatment	5 (0-10)	5 (0-10)	4.5 (0-10)	NS
initial RI ablation	4 (0-10)	5 (0-10)	4 (0-10)	0.012
whole body scanning	5 (0-10)	6.5 (0-10)	5 (0-10)	NS
thyroglobulin testing	6 (0-10)	8 (0-10)	5 (0-10)	NS
thyroid hormone withdrawal	5 (0-10)	8 (0-10)	5 (0-10)	0.008
Anxiety	5 (0-10)	5 (0-10)	5 (0-10)	NS
Depression	6 (0-10)	7 (0-10)	5 (0-10)	NS
Fear of: future diagnostic tests	5 (0-10)	5.5 (0-10)	5 (0-10)	NS
a second cancer	5 (0-10)	5 (0-10)	7 (0-10)	0.05
recurrence of cancer	5 (0-10)	5 (0-10)	3 (0-10)	0.028
metastases	3 (0-10)	5 (0-10)	2 (0-10)	0.048
Social well being	78.5 (20-129)	82.5 (43-129)	77 (20-125)	NS
Distress in family caused by illness	1 (0-10)	2 (0-10)	1 (0-10)	NS
Support from others	1 (0-10)	1 (0-10)	1 (0-10)	NS
Interference of illness with relationships	8 (0-10)	8.5 (0-10)	7 (0-10)	NS
Impact on sexuality	8 (0-10)	8 (0-10)	8 (0-10)	NS
Motivation to work	6 (0-10)	7 (0-10)	5 (0-10)	NS
Time away from work	7 (0-10)	8 (0-10)	6 (0-10)	NS
Productivity at work	7 (0-10)	7.5 (0-10)	6 (0-10)	NS
Quality of work	6 (0-10)	6.5 (0-10)	6 (0-10)	NS
Negative impact on: driving a car	9 (0-10)	9 (0-10)	9 (0-10)	NS
household chores	7 (0-10)	9 (0-10)	6 (0-10)	0.004
preparing meals	8 (0-10)	10 (3-10)	7 (0-10)	0.002
leisure activities	7 (0-10)	7 (1-10)	7 (0-10)	NS
Feeling of isolation	10 (0-10)	9.5 (0-10)	10 (0-10)	NS
Financial burden	6 (0-10)	6.5 (0-10)	5.5 (0-10)	NS
Spiritual well being	38 (10-70)	35 (13-60)	39.5 (10-70)	NS
Importance of religious activities	5 (0-10)	5 (0-10)	7 (0-10)	0.043
Importance of spiritual activities	2 (0-10)	1 (0-10)	2 (0-10)	NS
Changes in spiritual life	3 (0-10)	3 (0-10)	3 (0-10)	NS
Uncertainty about future	6 (0-10)	6 (0-10)	5.5 (0-10)	NS
Positive changes in life	5 (0-10)	5 (0-10)	5 (0-10)	NS
Feeling of purpose/mission in life	9 (0-10)	9 (0-10)	9 (0-10)	NS
Feeling hopeful	9 (0-10)	10 (0-10)	9 (0-10)	NS

*P value - NS: not significant

Table 4. Factors associated with physical, psychological, social and spiritual well being score of patients with thyroid carcinoma during levothyroxine withdrawal

Variables	No. of patients	Physical well being		Psychological well being		Social well being		Spiritual well being	
		Coefficient [§]	P	Coefficient [§]	P	Coefficient [§]	P	Coefficient [§]	P
Age (year)	150	-0.05	0.70	-0.07	0.78	-0.21	0.18	-0.09	0.21
Gender									
Male	36	10.9		13.2		8.1	0.09	–	
Female‡	114	referent	0.010	referent	0.06			–	
Follow-up‡	125	–		–		referent		–	
Radioablation	25	–		–		9.3	0.10	–	
Educational level									
Secondary‡	112	referent		referent		referent		–	
Tertiary	38	6.2	0.15	10.9	0.13	8.3	0.09	–	
TSH (mIU/L)*									
30 to 60‡	33	–		–		–		referent	
61-100	66	–		–		–		-6.15	0.025
>100	51	–		–		–		-3.16	0.016

[‡]Reference category; [§]Coefficient indicates the change of mean level of physical, psychological, social and spiritual well being score for an increase of 1 year for age, whereas for categorical variables indicates the difference between the mean of score and the respective reference categories. A positive coefficient indicates a better

The average score of psychological well being was 107 (range: 41 to 199) out of maximum 220 points. There were no significant differences by age, sex, education and TSH level. The analysis of patients' individual statements on the PSYWB scale (Table 3) showed that the leading difficulties were distress related to initial diagnosis (2, range: 0 to 10), distress caused by surgical treatment (3, range: 0 to 10), fear of metastases (3, range: 0 to 10) and stress caused by initial radioiodine ablation/treatment (4, range: 0 to 10). Women had significantly lower score than men on distress caused by initial radioiodine ablation/treatment (4, range: 0 to 10 vs 5, range 1 to 10; p=0.012, Mann-Whitney U test) and thyroid hormone withdrawal (5, range: 0 to 10 vs 8, range 1 to 10; p=0.008, Mann-Whitney U test). While men were more fearful of second cancer, women had more fear of recurrence of cancer and metastases.

The median social well being score was 78.5 (range: 20 to 129) out of maximum 140 points. Respondents with higher educational level achieved a significantly higher score than less educated patients (median: 81.5, range 21 to 129 vs. 78, range 20 to 125; p=0.026, Mann-Whitney U test) (Table 2). Illness was very distressing for their families (1, range: 0 to 10) and they reported insufficient support from others (1, range: 0 to 10), but they did not feel isolated (10, range: 0 to 10). Although the examinees did not report great interfering of illness and treatment with their activities at home, women had significantly lower score on statements about negative impact on household chores (6, range: 0 to 10 vs 9, range 0 to 10; p=0.037, Mann-Whitney U test), and preparing meals (7, range: 0 to 10 vs 10, range 3 to 10; p=0.004, Mann-Whitney U test) (Table 3).

In subscale related to spiritual well being the average score was 38 (range: 10 to 70) out of maximum 70 points. Patients reported that they felt very hopeful

(9, range: 0 to 10) and sensed a purpose/mission for their life (9, range: 0 to 10). The religious activities were significantly more important for women than men (7, range: 0 to 10 vs 5, range 0 to 10; p=0.043, Mann-Whitney U test) (Table 3).

Male patients had higher physical well being scores than female on multiple regression analysis (Table 4). Although respondents with higher educational level achieved a significantly higher social well being score than less educated patients on bivariate analysis after adjustment for age and other covariates in multivariate analysis there were no significant difference. After adjustment for age patients with higher TSH level had lower spiritual well being score on multiple regression analysis.

DISCUSSION

Successful application of radioiodine as well as thyroglobulin testing requires hypothyroid state which could be achieved either by stimulation of endogenous thyrotropin (TSH) production after withdrawal of levothyroxine therapy or by administration of recombinant TSH (rhTSH). An elevated TSH after thyroid hormone withdrawal leads to hypothyroid state that could be associated with the serious side effects which can have a negative impact on the patient's quality of life (Crevenna et al. 2003, Hassey-Dow et al. 1997). There are many definitions of quality of life (Crevenna et al. 2003, Hassey-Dow et al. 1997, Botella-Carretero et al. 2003). Quality of life (QOL) is defined as an individual perception of position in life, in relation to patient goals, expectations, standards and concerns (Crevenna et al. 2003). Today, in health researches, most commonly used definition is Health related quality of life which is defined by a multidimensional model that consists of

physical, psychological and social well-being. QOL has been extensively evaluated in differentiated thyroid cancer subjects during changes in circulating thyroid hormone levels for diagnostic and therapeutic purposes (Hassey-Dow et al. 1997, Botella-Carretero et al. 2003, Taieb et al. 2011). Therefore, we also tried to find which factors impact mostly on the quality of life of hypothyroid patients and obtained data could be used to improve the educational level of patients, their families as well as medical staff with the possibility of improving life quality through the positive impact of certain aspects of human well being.

In recent reports on QOL in thyroid carcinoma patients many questionnaires were used. Among most commonly used questionnaires are SF-36, SF-12, Nottingham Health Profile, University of Washington QOL questionnaire, QOL- Thyroid version Questionnaire, City of Hope (Crevenna et al. 2003, Hassey-Dow et al. 1997, Botella-Carretero et al. 2003, Dagan et al. 2004, Kung et al. 2006, Hoftijzer et al. 2008, Brearley et al. 2011). We decided to use QOL- Thyroid version Questionnaire, City of Hope because it is designed specifically for thyroid carcinoma patients, while other questionnaires were made for QOL in general. Patient's compliance with the test was fairly good (response rate 92.5%). The main problems encountered were incompleteness of the questionnaires, and only sometimes refusal to participate in the study because of inconvenience or lack of time, that is comparable with other studies (Lee et al. 2010).

According to different subscales, we expected the lowest results in subscale related to physical well being, which would be compatible to the recent reports on the quality of life after thyroid hormone withdrawal where a significant reduction in physical and psychological quality of life was observed (Hassey-Dow et al. 1997). The analysis of patient's individual statements on the physical (PHWB) subscale showed that our patients had most difficulties with fatigue, intolerance to cold and heat, sleep changes, and weight gain, but with higher average values than expected. As in other reports, fatigue was one of three most common physical difficulties (Davids et al. 2006). Female patients had significantly more difficulties than male respondents with following symptoms: fatigue, appetite changes, sleep changes, dry skin or hair changes, voice changes and swelling/ fluid retention but less with tolerance to cold and heat.

The individual statements based on the psychological (PSYWB) scale showed that the leading difficulties were distress related to initial diagnosis, distress caused by surgical treatment, fear of metastases and stress caused by radioiodine ablation. Women had significantly lower score than men on distress caused by initial radioiodine ablation/treatment and thyroid hormone withdrawal. Generally, women had more fear of recurrence of cancer and metastases. The leading difficulties in each group of questions remained mostly the same in other studies (Davids et al. 2006).

According to social well being, in our study, respondents with higher educational level achieved a significantly higher score than less educated patients. One another study has shown that there was a significant decrease in quality of life in poorer educated patients and in elderly (Tan et al. 2007). Furthermore, other studies have shown that variables such as education, religiosity and elapsed time interval since initial diagnosis were not correlated with depression and anxiety (Tagay et al. 2007). Other work has shown that education and occupation modified the effect of cancer on the employment; the difference between cancer survivors in the probability of being employed was greater in the lower than in the higher educational groups (Taskila-Abbrandt et al. 2004).

Generally, the examinees did not report severe interfering of illness and treatment with their activities at home. As expected, women had significantly lower scores on statements about negative impact on household chores and preparing meals which is understandable since women still do most of the housework in our community.

In subscale related to spiritual well being patients reported that they felt very hopeful and sensed a purpose/mission for their life. The religious activities were significantly more important for women than men, but all of them changes spiritual activities allowed them higher importance after establishing a diagnosis of malignant disease.

Male patients had higher physical well being scores than female on multiple regression analysis in our investigation. Although respondents with higher educational level achieved a significantly higher social well being score than less educated patients on bivariate analysis after adjustment for age and other covariates in multivariate analysis there were no significant difference. After adjustment for age patients with higher TSH level had lower spiritual well being score on multiple regression analysis. Since there are findings in the literature that describe better quality of life in patients younger than 45, male patients and patients with higher level of education (Dagan et al. 2004, Tan et al. 2007, Tagay et al. 2007, Taskila-Abbrandt et al. 2004), we expected similar findings in our study, but after dividing our patients into groups according to age, gender, current employment status, TSH level and reason for hospitalization we noted only difference in particular difficulties, mostly in gender groups. Similar findings were noted in another study (Dagan et al. 2004).

Most respondents indicated that their quality of life was quite good, in general. Illness was very distressing for their families but they did not feel isolated. Respondents also indicated a desire for adequate information about the disease, signs of recurrence, and recent developments in thyroid cancer treatment. Recent reports have also emphasized the need for more patient information and support (Roberts et al. 2008). Having that in mind, we should provide to patients access to

proper and complete information about their disease and, if possible, contacts of support groups.

In many reports most common difficulty is fatigue which reminds us that despite positive influence of psychological, spiritual and social well being, physical difficulties are still present and can cause QOL impairment in certain patients and disable normal daily functioning (Davids et al. 2006). In that case, some symptoms, mostly physical, could be diminished by using recombinant TSH and avoiding hypothyroidism (Schroeder et al. 2006). Recombinant human TSH is a source of exogenous TSH and its administration to thyroid cancer patients remaining on thyroid hormone therapy promotes radioiodine uptake by thyroid cells with the same efficacy as hypothyroidism but with preserving the patient's quality of life. More recently, the clinical benefits of the use of rhTSH versus thyroid hormone withdrawal on the preservation of QOL have been demonstrated (Lee et al. 2010, Schroeder et al. 2006). Because of the relatively high price of rhTSH its use is limited and sometimes not under reimbursement policy of health insurance. The second way to avoid these difficulties is possible reducing the period of hypothyroidism. The total TSH concentration in the serum of our patients were above the upper limit of normal values, which means higher than 30 mIU/L (normal range 0.40-4.2 mIU/L) that seems desirable for nuclear-medicine procedures in thyroid cancer patients. Moreover, the average value of TSH at the time of measurement in our patients after four weeks withdrawal were significantly higher, so in order to reduce the period of hypothyroidism with all unintended consequences this period could be shortened. According to the literature, the minimum required concentration of TSH absolute level of 30 mIU seems arbitrarily determined, and there are no data to describe the quality of scintigraphic display as well thyroglobulin testing and success of ablation as a function of the different concentration of TSH in serum (Medvedec 2006). Here, it seems also important to consider patient's age because it is observed that there is a rapid increase of TSH at a younger age, than in older patients, although this was not the subject of this research. For exploring reason, patients divided into three groups according to TSH level, and showed compatible results (Table 4). Likewise, we found no relationship between different values of TSH level between three groups of patient (>30-60, 60-100, and >100). Since the patients (at the time of four week withdrawal) multiple exceeded the recommended value (>30 mIU/L), it could be concluded that the target TSH value can be achieved in a shorter time than twice normal. Therefore, the value of TSH could be measured two weeks after omission of hormone replacement therapy and if the target value is reached immediately performed diagnostic and therapeutic procedures which would guarantee a significantly shorter average duration of hypothyroid condition of the patient. The modes of treatment (ablation or control) and different level of TSH did not affect a grade of

symptoms in this study. As in another study (Tagay et al. 2007) the TSH level as an indicator of hypothyroidism did not correlate with depression or with anxiety on a significant statistical level.

Despite these interesting findings, our study suffers from several possible limitations. First, it is limited by lack of comparison with a healthy control group and a lack of information regarding specific details about thyroid cancer stage as well as type of treatment. Further investigation with a larger number of ablation patients with more demographic and pathohistologic data is needed. Furthermore, the including of the healthy control group with normal values of TSH (euthyroid patients) with data comparison should be performed. The study was designed as a cross-sectional survey and as such did not allow any causative conclusions. Another limitation of the study could be the length of the questionnaire. It is possible that patients became tired after a number of questions and did not concentrate on the answer by the end of the test. Also, spiritual well being subscale had week internal consistency, hence the results of this score should be interpreted with caution. With these limitations in mind, we believe that our study provides evidence of high-risk areas in patients lives that are negatively affected by hormone withdrawal.

CONCLUSION

The impact of thyroid hormone withdrawal on QOL showed significant changes in physical, psychological, and social well-being across the four testing points. While it is generally known that patients have physical symptoms relating to thyroid hormone withdrawal, the greatest changes occurred in psychological (distress caused by initial diagnosis, surgery, ablation, fear of metastases), and social (distress in the family caused by illness) spheres that emerged as the strongest determinants for most of the domains in the questionnaire that could have a negative influence on global health. Improvement in quality of life in DTC patients can be achieved by directing our attention to specific areas of physical, social and psychological well being. Patients need to be encouraged to talk about their dilemmas and problems through active conversation with physicians who should provide a detailed explanation of the nature of their disease, possible difficulties and course of recovery. Physicians could help to improve QOL and reduce the increased anxiety among patients by informing and teaching them how to manage these uncomfortable symptoms with the possibility of development of educational groups. Since short-term hypothyroidism accounts for a substantial proportion of the QOL impairment, this situation could be improved by avoiding hypothyroidism and applying rhTSH instead. Data which has been obtained could be used to achieve a positive impact and better recovery of patients by directing our attention to most expressed difficulties noted in this questionnaire.

Acknowledgements: None.

Conflict of interest : None to declare.

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