Factors affecting the quality of life of well-differentiated thyroid carcinoma patients: A cross-sectional study on 435 Iranian patients

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ABSTRACT

Introduction: Differentiated thyroid carcinoma (DTC) is associated with excellent prognosis and high survival rates. This study was conducted to evaluate the influence of baseline and treatment-related factors on the health related quality of life (QoL) in cured DTC.

Methods: This study was an analytic cross-sectional study on radio-iodine (RAI) treated DTC patients during 2011-2012. The data on patients' QoL were recorded using a validated EORTC QLQ-C30 version 3.0. Also a checklist was used to record demographic data as well as information about the educational, marital and economic status. Duration of follow up, frequency of RAI therapies and number of surgeries were also recorded. General linear model multivariate analysis of variances (GLM-MANOVA) was used to analyze the data.

Results: Totally 435 DTC patients, 41.11±11.25 years, 77% female were assessed. Most of them were married (79%) and unemployed (57%). Global health and Qol as well as functional domains were better in women, single and higher educated patients. The QoL score in female cases was better in four functional subdomains, i.e physical, emotional, role and cognitive, but not for social functioning. QoL was adversely affected by increased number of radio-iodine therapies, radio-iodine cumulative doses and number of surgeries.

Conclusion: We found that quality-of-life scores are affected by the majority of socio-economic, treatment and follow-up variables. Attention to the quality of life and well-being of the patient as well as availability of professional support may be important aspects of the DTC patients' treatment and follow-up.

Key words: Quality of life; Differentiated thyroid carcinoma; Follow-up

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INTRODUCTION

The world health organization has declared health as a state of complete physical, mental and social well-being, not only absence of disease. This definition put emphasis on a novel meaning apart from absence of disease which is quality of life (QoL) [1]. QoL is influenced by the individual insight about the life, goals, expectations, standards, concerns and cultural context in which the patient lives. [2].

Most of patients with differentiated thyroid carcinoma (DTC) have good prognosis and higher survival rates [3]; however, the main aim of cancer treatment is not only to cure disease and to improve length of life but also to prolong a good quality of life (QOL) [2-4]. Indeed, the modern medicine put emphasis on the QoL of the survived patients.

The QoL in DTC patient is influenced by four processes, i.e. fear and hesitation related to cancer diagnosis, radical and partial surgical treatments, radioactive iodine therapy and the fluctuation in the thyroid hormone level and endocrine disorder [5].

Although there are many studies on thyroid cancer and quality of life [1-10], the obtained data is restricted because small sample size and general QoL questionnaires were used in such studies [5]. The aim of this study was to identify the main factors affecting the quality of life in DTC patients. This investigation was also aimed to recognize the predicting factors of DTC patient's QoL.

METHODS

Study design

This is an analytic cross-sectional study which was conducted during 2011-2012 in the Research Center for Nuclear Medicine, Shariati Hospital, as the national referral center for the treatment of thyroid carcinoma. Geographic distribution of the studied patients referred to our center is depicted in Table 1.

Table 1: Geographic distribution of the differentiated thyroid carcinoma patients referred to Research Center for Nuclear Medicine, Shariati Hospital, Tehran, Iran.

Geographic location*	Proportional Frequency
Tehran	30.6%
North and West of Iran	28.6%
Center of Iran	16.6%
East of Iran	14.6%
South of Iran	9.3%

*North and west provinces: Gilan, Mazandaran, Golestan, Azerbaijan (East and West), Ardebil, Kurdistan, Kermanshah, Lorestan, Ilam; Center provinces: Alborz, Qasvin, Zanjan, Hamedan,, Markazi, Semnan, Qom, Kohgiluyeh and Boyer-Ahmad, Chaharmahal and Bakhtiyari, Esfahan, Yazd; East provinces: Khorasan (South, Razavi, North), Sistan and Baluchestan; South provinces: Kerman, Fars, Khuzestan, Bushehr, Hormozgan.

The cytologically documented DTC patients were included in the study if they were older than 18 years and underwent total or near-total thyroidectomy and ablative radioactive iodine (RAI) therapy with a minimum interval of 6 months between initial treatment and evaluation dates.

The non-probability quota-sampling method was used according to gender (female/male ratio of 3 to 1) and age distribution of DTC patients in population. All patients were evaluated in euthyroid state and the cases with either mental or physical chronic illness influencing health related QoL such as diabetes mellitus, coronary artery disease, chronic renal failure, seizure, multiple sclerosis, rheumatic disease, cerebral-vascular disease, recent surgery (less than 6 months), bipolar manic depression disorder, major depression, schizophrenia, severe general anxiety or any other chronic diseases were excluded from the survey.

Data collection

The data collection process was done by a nuclear physician using the patient's files, pathology reports and via a structured interview.

Questionnaire items consisted of demographic and socio-economic characteristics such as age, gender, educational status (illiteracy/ elementary/ high school/ college or higher), marital status (single/ married/ divorced), career (employed/ unemployed), monthly income (none, low, middle and high). A structured check-list was also used to record the data about the disease status and treatment components such as the type of cancer (papillary/ follicular/ mixed), number of surgeries, number of RAI therapies, follow-up duration (months), cumulative dose of administered RAI and the frequency of recurrences.

Health- related quality of life assessment (HR-QoL)

The "European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30" (EORTC QLQ-C30) version 3.0 was used to assess the QoL in our study. EORTC QLQ-C30 is a cancer-specific 30 item questionnaire. It contains five functional domains (physical, social, role, cognitive and emotional), nine symptom scales (fatigue, nausea & vomiting, dyspnea, insomnia, appetite loss, constipation, diarrhea and financial difficulties) and a global health and QoL scale. All responses in this questionnaire are categorized in four levels, from "not at all" to "very much" except for two items of global health and quality of life which are classified with seven points from "very poor" to "excellent". Summative score is presented as 0 to

100. Although higher score of functional domains, global health and quality of life correspond to better quality of life, higher symptom scales means poorer QoL. The validated Persian account of EORTC QLQ-C30 (version 3.0) was applied in our study [11], using the QoL unit of the EORTC permission (http://www.eortc.be).

Statistical analysis

The data was analyzed according to the EORTC QLQ-C30 manual scoring. The quantitative variables were described using mean, median, range and standard deviation. The General linear model multivariate of variance (GLM-MANOVA) approach was used to test the hypothesis of a significant association between a set of interrelated dependent variables (HR-QoL scales) and independent variables (socio-demographic, clinical and treatment data). As the first step, univariate analyses, i.e. paired t-test, analysis of variance (ANOVA), Pearson's and spearman correlations were applied to compare data in study subgroups. As the second step, the associated factors were entered into the GLM model. All statistics were considered significant at the level of $p < 0.05$.

RESULTS

Totally 460 well differentiated thyroid carcinoma patients were included and 435 patients were studied (response rate: 94.5%).

The mean age of participants was 42.11 ± 14.25 years (18-83 years). Most of patients were female (77%), married (79.3%), high school graduated (43.7%), unemployed (57.5%). Disease and treatment characteristics are depicted in Table 2.

Table 2: Socio-demographic, clinical and treatment characteristics of participants.

Variables		Frequency (%)
Gender	Male	98 (22.7)
	Female	337 (77.7)
Marital status	Married	343 (79.3)
	Single	92 (20.7)
Educational status	Illiteracy	78 (18.6)
	Elementary	77 (18.4)
	High School	187 (43.7)
	College & Higher	93 (19.3)
Career status	Employed	184 (42.3)
	Unemployed	251 (57.7)
Individual income*	Low	271 (62.5)
	Medium	131 (30.3)
	High	32 (7.2)
Frequency of radio-iodine therapies	<2	12 (2.8)
	2-5	348 (80)
	5-8	58 (13.5)
	>8	17 (3.7)
Number of surgeries	<2	224 (51.7)
	2-4	197 (45.3)
	>4	14 (3%)
Follow-up duration (years)	<5	337 (77.7)
	5-12	66 (15.2)
	>12	32 (7.1)
DTC pathologic type	Papillary	388 (89.5)
	Follicular	47 (10.5)

*On the basis of monthly income (million Rials) Low: less than 6, Medium: 6-25, High: more than 25.

As well, the score of each domain is shown, as mean and standard deviations, in Table 3.

Table 3: Descriptive results of EORTC QLQ-C30 version 3.0 domains.

	Mean ± SD	Median(range)
Functional domains		
Physical functioning	87.6 ± 17.2	81.7(0-100)
Role functioning	86.65 ± 20.3	79.9(0-100)
Emotional functioning	55.27 ± 18.7	51.12(33-100)
Cognitive functioning	78.77 ± 15.8	67.01(33-100)
Social functioning	96.52 ±16.23	93.3(33-100)
Symptom scale		
Fatigue	29.98 ± 22.4	27.2 (0-100)
Nausea/vomiting	10.45 ± 1.96	10.1 (0-75)
Pain	21.12 ± 16.12	18.9 (0-100)
Dyspnea	17.92 ± 9.6	15.89 (0-100)
Insomnia	28.04 ± 11.7	26.1 (0-100)
Appetite loss	19.7 ± 1.29	18.67 (0-100)
Constipation	16.62 ± 2.52	11.45 (0-75)
Diarrhea	22.31 ± 11.2	19.9 (0-100)
Financial difficulties	40.99 ± 23.1	38.1 (0-100)
Global health and quality of life	68.72 ± 19.7	61.24 (0-100)

The results of univariate analysis for the factors affecting functional subdomains of QoL are demonstrated in Table 4.

The associated factors with symptom scale and global health in DTC patients are described in Table 5. As noted in the tables, female cases had better QoL in all functional domains and symptom scales except for social functioning. Education status, number of radio-iodine therapies, number of surgeries, follow-up period and cumulative dose of radioactive iodine therapies were associated with QoL.

To analyze the correlations between the factors and the QoL scales, general linear model (GLM) multivariate analysis of variances (MANOVA) was used and the results are shown in Table 6.

DISCUSSION

In the current study, we tried to evaluate the association of "quality of life" with socio-demographic and clinical factors in RAI-treated DTC patients. In the field of functional domains, social functioning shows the highest and the emotional functioning reveals the worst scores. The worst symptom scale is fatigue. The most effective factors on QoL in our study are age, gender, educational, marital and career status as well as the frequency of RAI therapies, number of surgeries and cumulative radioactive iodine doses. Older age, male gender, well-educated, married (vs. single or divorced) and employed (vs. unemployed) patients reveal better QoL. Gender, age and marital status have also been evaluated as possible factors affecting QoL in other studies [1-10].

Table 4: Association of functional subdomains of "quality of life" with socio-demographic and clinical variables.

	Physical	Emotional	Cognitive	Social	Role
Gender*					
Female	90.1±10.8	72.75±20.16	86.41±11.41	97.01±25.22	87.14±9.43
Male	76.7±14.2	50.17±31.4	58.4±25.02	95.5±24.23	70.26±21.55
p-value	0.001	0.021	0.003	0.139	0.021
Marital status*					
Single	84.5±21.27	70.3±26.36	61.11±23.27	55.14±25.07	90.27±6.49
Married	78.51±22.4	70.9±27.87	71.4±14.9	50.01±27.16	81.68±8.59
p-value	0.42	0.89	0.076	0.97	0.069
Educational status*					
Illiteracy	72.68±8.28	72.1±21.7	33.1±17.81	70.5±11.22	88.18±7.2
High school and more	86.66±10.14	81.00±12.2	40.1±22.2	72.1±10.2	91.27±4.6
p-value	0.041	0.04	0.064	0.48	0.45
Career status*					
Employed	76.66±21.45	90.09±5.3	67.2±27.67	79.8±15.3	85.2±9.8
Unemployed	75.86±18.8	89.3±7.8	42.7±28.2	65.01±17.6	84.1±11.5
p-value	0.83	0.75	0.047	0.76	0.43
Individual income▪					
Low	81.86±12.1	81.49±8.9	53.2±15.3	95.8±5.8	73.5±16.9
Middle to high	87.52±9.01	95.7±11.2	62.3±10.6	96.01±8.1	78.04±14.7
p-value	0.62	0.078	0.92	0.99	0.056
Number of RAI therapies ◊	-0.19	-0.318	-0.021	-0.408	-0.009
p-value	0.058	0.01	0.062	0.005	0.516
Number of surgeries◊	-0.01	-0.01	0.000	-0.32	0.04
p-value	0.208	0.157	0.695	0.013	0.59
Follow-up duration (years)◊	-0.42	-0.032	-0.11	-0.21	-0.11
p-value	0.018	0.21	0.087	0.060	0.081
Cumulative dose (mCi) ◊	-0.11	-0.002	-0.01	-0.250	-0.019
p-value	0.078	0.87	0.695	0.028	0.59

*mean ± standard deviation, independent t-test; ▪On the basis of monthly income (million Rials) Low: less than 6, Medium: 6-25, High: more than 25 using analysis of variances (ANOVA), post hoc: Schefe; ◊ Pearson's correlation.

Table 5: Association of symptom scale and global health with socio-demographic and clinical variables.

	Fatigue	Nausea/vomiting	Pain	Dyspnea	Insomnia
Gender*					
Female	32.1±25.27	13.2±8.9	26.41±20.01	31.64±22.62	21.99±13.17
Male	22.47±19.24	11.5±6.18	16.49±13.19	15.12±13.3	12.07±10.6
p-value	0.001	0.01	0.001	0.0032	0.005
Marital status*					
Single	32.78±25.81	21.52±16.2	21.51±20.17	27.61±20.97	28.59±20.9
Married	28.95±23.8	25.4±15.8	24.44±24.04	32.01±29.46	21.28±18.03
p-value	0.121	0.127	0.153	0.396	0.028
Educational status*					
Illiteracy	43.35±36.57	25.97±16.17	18.5±11.2	24.32±20.7	31.9±27.6
High school and more	36.16±30.5	21.01±16.4	14.4±7.3	22.8±16.26	29.77±24.6
p-value	0.124	0.004	0.02	0.348	0.656
Career status*					
Employed	22.2±16.8	22.2±12.5	19.3±15.5	24.5±20.0	24.3±19.8
Unemployed	32.8±25.6	19.5±12.5	29.3±26.8	34.26±20.9	24.5±20.0
p-value	0.65	0.42	0.051	0.051	0.058
Individual income▪					
Low	25.9±21.8	13.2±7.07	22.05±18.5	21.25±18.89	24.81±18.43
Middle	30.1±21.5	16.5±8.06	18.43±18.27	25.8±23.9	23.8±15.9
p-value	0.881	0.083	0.089	0.79	0.24
Number of RAI therapies ◊	0.21	0.38	0.021	0.019	0.015
p-value	0.05	0.031	0.078	0.082	0.100
Number of surgeries◊	0.28	0.36	0.3	0.32	0.18
p-value	0.01	0.031	0.026	0.019	0.06
Follow-up duration (years)◊	-0.17	-0.019	0.07	0.04	-0.021
p-value					
	0.062	0.091	0.59	0.695	0.09
Cumulative dose (mCi)◊	0.019	0.18	0.021	0.02	0.29
p-value	0.09	0.058	0.085	0.087	0.028

*mean ± standard deviation, independent t-test; ▪ On the basis of monthly income (million Rials) Low: less than 6, Medium: 6-25, High: more than 25 using analysis of variances (ANOVA), post hoc: Schefe; ◊ Pearson's correlation.

Table 5: Association of symptom scale and global health with socio-demographic and clinical variables (**Continued**).

	Appetite loss	Constipation	Diarrhea	Financial difficulties	Global health/QoL
Gender*					
Female	29.17±21.99	29.82±19.7	29.8±13.8	39.22±25.37	65.88±23.69
Male	27±12.07	26.81±15.45	22.4±10.99	41.58±23.92	56.16±24.69
p-value	0.21	0.203	0.071	0.403	0.0001
Marital status*					
Single	28.59±20.9	25.78±14.4	25.03±12.7	37.4±31.7	76.24±28.2
Married	27.25±19.03	28.7±19.5	29.12±12.23	41.54±32.4	52.29±31.9
p-value	0.241	0.153	0.459	0.982	0.011
Educational status					
Illiteracy	28.5±20.4	28.4±18.4	28.92±13.2	42.35±36.57	52.2±13.99
High school	25.06±17.06	28.43±19.4	25.3±13.05	36.16±30.5	64.4±23.2
p-value	0.773	0.98	0.838	0.008	0.004
Career status					
Employed	33.01±28.8	33.01±17.7	24.04±13.06	24.55±20.0	60.5±19.1
Unemployed	29.8±22.8	29.6±20.5	24.12±11.11	41.06±25.39	57.2±11.77
p-value	0.480	0.110	0.720	0.024	0.097
Individual income▪					
Low	23.21±13.13	26.5±17.42	35.82±12.87	44.69±17.9	67.1±11.3
Middle	26.99±18.27	25.63±17.2	22.4±13.97	33.33±13.03	69.2±12.01
p-value	0.95	0.54	0.058	0.069	0.087
Number of RAI therapies ◊	0.023	0.023	0.12	0.10	-0.011
p-value	0.082	0.084	0.061	0.069	0.85
Number of surgeries◊	0.18	0.39	0.29	0.05	-0.38
p-value	0.06	0.018	0.031	0.173	0.004
Follow-up duration (years) ◊	0.017	0.01	0.009	0.11	-0.09
p-value	0.212	0.11	0.524	0.065	0.98
Cumulative dose (mCi)◊	0.017	0.019	0.021	0.029	-0.11
p-value	0.089	0.084	0.061	0.069	0.42

*mean ± standard deviation, independent t-test; ▪ On the basis of monthly income (million Rials) Low: less than 6, Medium: 6-25, High: more than 25 using analysis of variances (ANOVA), post hoc: Schefe; ◊ Pearson's correlation.

Table 6: Association of different demographic, socio-economic and clinical variables with "quality of life" of differentiated thyroid carcinoma patients (on the basis of a multi-factor model (general linear model multivariate of variances).

Variables	Wilk's λ[#]	Significance*(p value)
Demographic		
Age: <40y vs. 40-60y vs.>60y	0.929	0.0001*
Gender: female vs. male	0.949	0.023*
Socio-economic		
Educational status: high graduated vs. elementary	0.946	0.001*
Marital status: single vs. married	0.961	0.034*
Career: employed vs. unemployed	0.888	0.036*
Individual income: high vs. low and middle	0.984	0.715
Clinical and treatment data		
N. of Radioactive iodine therapies: <2 times vs. 2-5 vs. >5	0.932	0.019*
N. of surgeries: <2 times vs. 2-4 vs. >4	0.919	0.004*
Cumulative dose	0.942	0.045[Δ]

* The first values are associated with higher "quality of life" score; [Δ] The lower values are associated with higher "quality of life" score; [#] Variables were entered as independent variables in the model.

A prominent finding of our study is that female gender is associated with higher score in functioning domains of QoL (i.e. better QoL), while this association is not confirmed by the previous studies (1-3). The disparity between the results can be explained by the different cultures as well as inequality of the role and social characteristics of women between developed and developing countries. The influence of age, marital status and other socio-demographic factors are settled in different studies [5-9]. In some studies, older age at the time of initial diagnosis and treatment was associated with worse QoL, the finding that is also established in our study (5).

As a general result in our study, the increasing number of RAI therapies, surgeries and follow-up duration are associated with decrease in some functioning subdomains of QoL. In this regard, functional domains are less affected by the number of surgeries. In fact, the social functioning is the only functional subdomain deteriorated by increasing the frequency of surgeries while symptom scale is more

robustly affected by this factor. The total QoL score is also affected by the number of RAI therapies as this factor significantly influence the physical, emotional and social aspects of functioning in DTC patients. The previous studies has applied variable data tools, and evaluated other aspects of QoL, thus most of our findings, in-detail, are not comparable with the previous reports and further studies are needed to confirm our findings; however, our findings are completely logic and in-general are comparable with previous studies. In addition, complementary studies are recommended which consider the interval between surgery and assessment of QoL as independent factors affecting the QoL. In our study, entire follow-up duration was confirmed to have an adverse impact on physical subdomain of "QoL". In a similar study, Hoftijzer *et al.* reported that DTC patients following thyroidectomy and RAI therapy had a decrease in QOL when compared to the healthy controls using multiple questionnaires (SF-36, MFI-20, HADS, SDQ). They reported that HR-QoL may be returned to normal level after 12-20 years of follow-up, irrespective of the other clinical factors such as surgeries and RAI therapies (8). The absence of a long-term prospective reassessment of "QoL" is one of our study restrictions.

Tagay *et al.* study showed that depression and anxiety in patients with DTC are correlated with QoL. The most significant determinants for depression and anxiety were social support and coherence; whereas TSH level did not show a statistically significant association with depression or anxiety [12]. These findings can be considered in the future studies on QoL in well differentiated thyroid cancer patients.

Using EORTC QLQ-C30 version 3.0 as a cancer-specific health-related quality of life questionnaire [5] and the large sample size are strength points of our study. Since the study was done in a referral center, the study sample can be a proper representative for well-differentiated thyroid cancer patients' population.

Two of three main destruction processes affecting QoL were studied in our study, i.e. fear and uncertainty related to cancer diagnosis, radical and partial surgical treatment and RAI therapy but as a remarkable limitation point of this study the fluctuating thyroid hormone level and endocrine disorder were not considered in this study; however, this was a cross-sectional study and we recommended a cohort or quasi-trial (before-after) study to control the other cofactors that may influence the QoL. We also recommended the grouping study between nuclear medicine and psychology centers to assess the combination effects of therapy and psychological disorders.

CONCLUSION

Male gender and higher age groups as well as the number of RAI therapies, number of surgeries and cumulative RAI dose adversely affect the "quality of life" of DTC patients. The "quality of life" score was also lower in different subgroups of DTC patients such as married, low-educated and unemployed subjects.

Acknowledgments

REFERENCES

1. Pelttari H, Sintonen H, Schalin-Jäntti C, Välimäki MJ. Health-related quality of life in long-term follow-up of patients with cured TNM Stage I or II differentiated thyroid carcinoma. Clin Endocrinol (Oxf). 2009 Mar;70(3):493-7.

2. Giusti M, Melle G, Fenocchio M, Mortara L, Cecoli F, Caorsi V, Ferone D, Minuto F, Rasore E. Five-year longitudinal evaluation of quality of life in a cohort of patients with differentiated thyroid carcinoma. J Zhejiang Univ Sci B. 2011 Mar;12(3):163-73.

3. Wan Leung S, Lee TF, Chien CY, Chao PJ, Tsai WL, Fang FM. Health-related quality of life in 640 head and neck cancer survivors after radiotherapy using EORTC QLQ-C30 and QLQ-H&N35 questionnaires. BMC Cancer. 2011 Apr 12;11:128.

4. Zebrack BJ, Yi J, Petersen L, Ganz PA. The impact of cancer and quality of life for long-term survivors. Psychooncology. 2008 Sep;17(9):891-900.

5. Husson O, Haak HR, Oranje WA, Mols F, Reemst PH, van de Poll-Franse LV. Health-related quality of life among thyroid cancer survivors: a systematic review. Clin Endocrinol (Oxf). 2011 Oct;75(4):544-54.

6. Malterling RR, Andersson RE, Falkmer S, Falkmer U, Niléhn E, Järhult J. Differentiated thyroid cancer in a Swedish county--long-term results and quality of life. Acta Oncol. 2010 May;49(4):454-9.

7. Lee JI, Kim SH, Tan AH, Kim HK, Jang HW, Hur KY, Kim JH, Kim KW, Chung JH, Kim SW. Decreased health-related quality of life in disease-free survivors of differentiated thyroid cancer in Korea. Health Qual Life Outcomes. 2010 Sep 15;8:101.

8. Hoftijzer HC, Heemstra KA, Corssmit EP, van der Klaauw AA, Romijn JA, Smit JW. Quality of life in cured patients with differentiated thyroid carcinoma. J Clin Endocrinol Metab. 2008 Jan;93(1):200-3.

9. Taïeb D, Sebag F, Cherenko M, Baumstarck-Barrau K, Fortanier C, Farman-Ara B, De Micco C, Vaillant J, Thomas S, Conte-Devolx B, Loundou A, Auquier P, Henry JF, Mundler O. Quality of life changes and clinical outcomes in thyroid cancer patients undergoing radioiodine remnant ablation (RRA) with recombinant human TSH (rhTSH): a randomized controlled study. Clin Endocrinol (Oxf). 2009 Jul;71(1):115-23.

10. Tan LG, Nan L, Thumboo J, Sundram F, Tan LK. Health-related quality of life in thyroid cancer survivors. Laryngoscope. 2007 Mar;117(3):507-10.

11. Safaee A, Moghim Dehkordi B. Validation study of a quality of life (QOL) questionnaire for use in Iran. Asian Pac J Cancer Prev. 2007 Oct-Dec;8(4):543-6.

12. Tagay S, Herpertz S, Langkafel M, Erim Y, Freudenberg L, Schöpper N, Bockisch A, Senf W, Görges R. Health-related quality of life, anxiety and depression in thyroid cancer patients under short-term hypothyroidism and TSH-suppressive levothyroxine treatment. Eur J Endocrinol. 2005 Dec;153(6):755-63.