

## QUALITY OF LIFE IN THYROID CANCER PATIENTS: A LITERATURE REVIEW

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### Abstract

**Introduction.** *Quality of life (QoL) has received increasing interest in the last years, especially in patients with cancer. This article aims to analyze a selection of medical research papers regarding the quality of life in patients with thyroid carcinoma. We overviewed the main QoL aspects derived from several studies and highlighted those less researched issues, which could represent a solid base for future clinical studies.*

**Method.** *We used an integrative selection method of medical literature, choosing mostly “free access” studies, as it was considered that they could be easily viewed, searched and researched including by patients.*

**Results.** *After an integrative literature review, we selected 16 relevant studies. Patients with thyroid cancer have several factors influencing their QoL, with both physical and psychological impact. The decisive factors are the quality of the surgical act, radioiodine therapy, follow-up using rh-TSH vs. hormonal withdrawal, access to behavioral help and the relationship with their physician.*

**Conclusion.** *We must understand the emotional impact of the cancer diagnosis on the patient and we must collaborate in order to help the patient restore the psychosomatic balance and to recover the quality of life*

**Keywords:** thyroid neoplasms, quality of life, iodine radioisotopes

### Introduction

The thyroid is an important endocrine gland, playing a major role in the normal functioning of almost all metabolic processes. The thyroid pathology is complex, comprising a benign element (which can coexist with other pathologies), but also a malignant element having a devastating impact on the patient [1]. Stress is a triggering factor of the autoimmune thyroid pathology, being also an element that accompanies the patient diagnosed with thyroid cancer [2].

Thyroid cancer is the most common endocrine

neoplasia: its incidence is growing at a global level, particularly due to papillary thyroid cancer, with emphasis on the early stages of disease, and thyroid incidentaloma [3]. It is well known that the incidence of thyroid cancer is higher in women than in men. However, men are generally going to the physician in a more advanced stage of disease, presenting extra-thyroidal extension, thus leading to a more reserved prognosis on both survival and recurrence rate of the disease.

The main causes of the increasing number of new cases of thyroid cancer in the last decade are: radiation (ionizing radiation), environmental factors, genetic factors, better access of the population to health services with increased addressability, and the development of medical

imaging with early detection of any changes in the thyroid gland [3]. So far, a global screening program to detect thyroid cancer has not been developed. Although the incidence increased, the mortality caused by this cancer has remained low.

Communicating the diagnosis of cancer attracts the idea of incurability, even if in the case of differentiated thyroid neoplasia the prognosis is as good as it can be. In 1987, Greer and Watson [4] identified four types of reactions of cancer patients when finding out the diagnosis: facing the situation, the belief of healing, the alteration of the health status and the denial. The patient is aware that future therapies to restore the somatic and psychological balance can be debilitating, and it is here that the refusal of the disease existence appears, and implicitly the difficulties in managing this type of patient. The symptoms and treatment of cancer generally entail a series of profound changes in the mental/psychological ability of the patient, in the social role he exercises in the society, in his personal life, and not least in everything involving the appearance. The vast majority of clinical trials have sought to identify anxiety and depression (psychological morbidity) as indicators of the quality of life of these patients [4].

Another approach towards the diagnosis is the revolt against cancer and this entails a series of questions and the uncontrolled desire in seeking answers, often in people who are unqualified to respond. The inconsistent information from virtual environments is perhaps the most difficult part to manage in the dialogue with cancer patients. The most challenging aspect is changing a patient's perspective on his disease and gaining his confidence, especially if he is misinformed. We often prefer an "ignorant" but confident patient than a so-called "well-informed" patient from inadequate sources.

According to the World Health Organization (WHO), the quality of life is defined as the perception of people of their position in life, in relation to their goals and value system which they have accepted and incorporated into the perspective of decisions that they make. The quality of life in medicine means physical, mental and social well-being, as well as the patients' ability to perform ordinary tasks in their daily existence (WHO 1998). This wording considers a slightly more specific concept, namely the quality of life in relation to health, which is the subjective health status and the impact this perception has upon his life abilities. As a concept, the quality of life in relation to health incorporates both positive and negative aspects of physical, mental and social health.

The current article includes and analyzes several key papers from medical literature regarding the quality of life in patients with thyroid cancer. We aim to find the most important factors influencing QoL in these patients and to highlight less known issues, which could represent a solid base for future clinical studies.

## Material and method

We used an integrative selection method of medical literature, choosing most of the studies from "open access" journals, due to their high approachability, but with an impact factor over 1.0 in the last two years.

In order to perform a reproducible search, we used a number of terms, keywords: "quality of life", "thyroid cancer". The main engines and search databases used included: MEDLINE / PubMed and ScienceDirect. We adjusted the search filters for years to 2008-2016.

At a first PubMed search using "quality of life in thyroid cancer" we identified 426 articles. Filters were applied on the type of article - original article. Therefore, we selected only the articles that concerned the approached theme: quality of life in patients with thyroid neoplasia. Regarding ScienceDirect database, by using the "quality of life in thyroid cancer," we identified 19 205 articles. We applied the filters related to the years of publication (2008-2016), the topics (patient, cancer, thyroid), the final number being of 105 articles to be reviewed. We selected only the articles which studied the quality of life in thyroid cancer, and we removed from the selection PubMed indexed articles that were already included in the study. We applied the following exclusion criteria: articles written in another language than English, abstracts without articles, editorials, articles published before 2009 and articles that are not scientifically validated through psychometric tools or that are poorly designed.

## Results

After an integrative literature review we selected 16 studies. Reading the included articles we identified some aspects related to the quality of life in thyroid cancer patients which were grouped according to the similarities between the studies:

- Quality of life and hormonal balance;
- Quality of life related to surgery (total thyroidectomy and lymphadenectomy);
- Quality of life in patients which are candidates to RAI (radioiodine ablation);
- Quality of life according to some demographic aspects (children/young adults, patients from different parts of the world- Korea, Puerto Rico);
- Psychosomatic interventions and behavioral help to improve the quality of life in thyroid cancer patients.

All the details regarding the 16 studies reviewed are integrated in Table I.

**Table I.** The 16 studies selected for the literature review on quality of life patients with thyroid cancer.

Author	Year	Country	Number of patients	Measurement instrument	Outcome measure	Study conclusion
Patrícia dos Santos Vigário et al. [5]	2013	Brazil	82 pts.	WHOQOL-Bref;	Exercise and QoL	Exercise seems to minimize the adverse effect of the treatment on QoL and HRQoL
Eva-Maria Gamper et al. [6]	2015	Austria, German, Nederland	439 pts.	EORTC QLQ-C30	Health and QoL	DTC patients' burden from symptoms and functioning impairments is unrelated to the favorable clinical outcome.
H. Duan et al. [7]	2015	Austria	session of a physician-only meeting	Physician's view; psychologist's view; patient's view	Medical treatment and QoL	Patients appreciate being asked about all the aspects of QoL
Yuri Choi et al. [8]	2014	Korea, USA	97 pts.	DLQI and VSS score	Surgical scars and QoL	Post-thyroidectomy scars on the neck affect the QoL of thyroid cancer patients regardless of scar type.
Rossen S. Dimov [9]	2013	Bulgaria	Literature review	QoL (quality of life)	Lymphatic spread and QoL	Cancer treatment must increase survival but also preserve QOL
Mateja Rubic et al. [10]	2014	Croatia	150 pts	Quality of life - Thyroid version (QOLTV) questionnaire,	Factors impacting QoL	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.
Birte Nygaard et al. [11]	2013	Denmark	56 pts.	SF-36; VAS (visual analogue scale)	QoL in patients undergoing hormonal withdrawal vs. rh-TSH treatment	The effect of rh-TSH compared to L-T 3 THW on QOL in DTC patients; a significant difference was demonstrated, though smaller than described in previous non-blinded studies.
Anna M. Sawka et al. [12]	2009	Canada	16 pts	3 focus groups sessions, a qualitative study	QoL in the diagnosis of thyroid carcinoma	The diagnosis and treatment of thyroid cancer significantly impacts the lives of survivors.
David Taïeb et al. [13]	2011	France	83 pts.	FACIT	QoL after the initial radioiodine therapy	The use of radioiodine ablation does not seem to affect the medium term QOL scores of patients. Medium-term QOL is mainly determined by pre-ablation QOL
Hong-Xia Wu et al. [14]	2016	China	60 pts.	QLQ-C30, SDS and SAS	the effects of psychological and behavioural intervention on QoL	Psychological and behavioural interventions for patients with DTC undergoing RAI facilitated positive outcomes.
Torquil Watt et al. [15]	2010	Denmark	907 pts.	ThyPRO- QoL (quality of life)	QoL evaluation through ThyPRO	The ThyPRO questionnaire is ready to use in clinical studies of patients with thyroid diseases
Youjin Jeong et al. [16]	2015	Korea	227 pts.	THYCA-QoL; Korean version of Quality of life EORTC QLQ-C30; BFI-K; BEPSI-K; Goldberg short screening scale for Anxiety and Depression; PHQ-9	validation of THYCA-QoL questionnaire in Korea	the questionnaire is reliable, valid, and suitable for use in primary care settings for measuring the HRQoL of Korean-speaking thyroid cancer survivors.
Ji In Lee et al. [17]	2010	Korea	316 pts	(EORTC QLQ-C30); (BFI); (HADS)	QoL in disease-free survivors of DTC	disease-free survivors of DTC experience a significantly decreased HRQoL.
Melanie Metallo et al. [18]	2016	France	45 pts.	SF-36 v2; ISP-25	QoL in young female survivors with DTC	quality of life of young female thyroid cancer survivors is not affected
Massimo GIUSTI et al. [19]	2011	Italy	128 pts. DTC 219 pts benign pathology	TQ; HAM-A; HAM-D; KSQ; MMSE	independent QoL evaluation	study confirms a wide variation in illness perception in DTC subjects, which is generally unrelated to the favourable clinical follow-up of the disease.
Mónica A. Vega-Vázquez et al. [20]	2015	Puerto Rico	75 pts.	Spanish version of the UW-QOL questionnaire	QoL in Puerto Rican patients with DTC	an overall minimal effect on their quality of life.

Legend: WHOQOL-Bref (the world health organization quality of life); EORTC QLQ-C30 (European Organization for Research and Treatment of Cancer, the Quality of Life Questionnaire-core30); DLQI (dermatology life quality index), VSS score (Vancouver scar scale score); QOLTV (Quality of life Thyroid version questionnaire); SF-36 (medical outcomes study 36 item short form health survey); VAS (visual analogue scale); FACIT (Functional assessment of chronic illness and therapy); QLQ-C30 (quality of life 30 core questionnaire), SDS (self-rating depression scale), SAS (self-rating anxiety score); THYCA-QoL Korean version (Korean version of the thyroid cancer-specific quality of life questionnaire); BFI-K (Korean version of brief fatigue inventory); BEPSI-K (Korean version of brief encounter psychosocial instrument); Goldberg short screening scale for Anxiety and Depression; PHQ-9 (a nine-item patient health questionnaire); BFI (brief fatigue inventory); HADS (hospital anxiety and depression scale); SF-36 v2 (medical outcomes study 36 item short form health survey); ISP-25 (25-item inventory of self physique); TQ (thyroid questionnaire); HAM-A (Hamilton's tests for anxiety); HAM-D (Hamilton's tests for depression); KSQ (Kellner symptom questionnaire); MMSE (minima mental state examination); Spanish version of the UW-QOL questionnaire (Spanish version of the University of Washington quality of life question).

Regarding the quality of life in thyroid cancer patients we selected some studies in which the authors demonstrated that the thyroid hormonal imbalance and the thyroid hormone withdrawal or the use of rh-TSH can influence the quality of life.

Mateja Rubic et al. [10] evaluated 150 patients to identify which factors impact mostly on life quality of patients with DTC after thyroid hormone withdrawal. Every patient responded to the quality of life thyroid version questionnaire with questions about physical, psychological, social and spiritual well-being. The most important factors influencing quality of life seem to be under covered by the physical symptoms after thyroid hormone withdrawal, but the fatigue, intolerance to cold or heat, sleep changes and weight gain had also very high scores in the questionnaire. They concluded that the thyroid questionnaire helped the physician to identify those aspects in patients' lives which are the most affected during thyroid hormone withdrawal.

Birte Nygaard et al. [11] undertook a study published in the European Thyroid Journal, a randomized blind placebo control study on the effect of recombinant human thyrotropin (rh-TSH) on the quality of life in the treatment of thyroid cancer. They wanted to see if there was any difference between using the rh-TSH method and the classical thyroid hormone withdrawal. This study included 57 patients, which had their quality of life assessed through the SF-36 questionnaire. They also had to rate their mood on two visual analogue scales, one at baseline and one during radioiodine therapy. The study found a significant difference of the quality of life between the group of patients undergoing rh-TSH therapy and the group who followed hormonal withdrawal, both on the questionnaire and on the visual analogue scales.

Surgical intervention followed by lymphadenectomy leave the patient with a scar which is very difficult to get used to, especially because it remains very exposed for the rest of the life, right in the centre of the neck. This is even

more difficult when the patient is a woman and the physical appearance is going down. We revised the literature and according to the filters we used in the searching strategy we found 2 studies that revised the quality of life in thyroid cancer patients according to the postsurgical scar.

The first study described comes from Korea, in which Yuri Choi et al. [8] wanted to evaluate the post-thyroidectomy scar on quality of life in thyroid cancer patients. He enrolled 97 patients who were categorized on the scar type: linear flat scars, linear bulging scars, hypertrophic scars or adhesive scars. The quality of life was evaluated using Dermatology Life Quality Index (DLQI) and the scars were graded according to Vancouver scale score (VSS). They found that DLQI scores did not differ among scar types but the post-thyroidectomy scars on the neck do influence life quality among these patients. They tried to make the surgical community to pay attention on the psychological effects of the scars and try to minimize them.

Rossen Dimov [9] from Bulgaria published a review article in Gland Surgery about the effect of neck dissection on the quality of life in patients with differentiated thyroid cancer. The conclusion of the review is that the neck dissection influences the quality of life in two main directions: positive and negative. The positive direction is linked to an appropriate neck dissection, which represents the main goal of the surgical therapy. The other way, the negative one, is determined by a faulty surgical act and postoperative complications, influencing the overall quality of life.

All the physicians involved in the therapy of thyroid cancer including radioiodine therapy had encountered difficulties regarding the management of the psychological effects in these patients; effects that rise from the insufficient and unclear information regarding this procedure. There are a lot of misinformed patients that spread wrong, faulty information to other patients in the waiting room. Thus, the mystery of the iodine procedure and the idea that everyone is a little "bomb" develops in time a lot of fears that are very difficult to treat and that influence in a negative way the health-related quality of life of the DTC patients. When we reviewed the medical literature we found some studies on this theme.

The qualitative study of Anna Sawka et al. [12] from Canada on the impact of thyroid cancer and post-surgical radioactive iodine treatment on the lives of thyroid cancer survivors was conducted in three focus group sessions with 16 participants (12 women and 4 men) with radioiodine treatment according to the medical history. They reported in the group sessions that having a diagnosis of cancer is life-changing with a lot of fears and uncertainty. Part of the patients also reported receiving insufficient information on their disease or conflicting messages from health-care providers. The conclusion on the qualitative study resemble in that the diagnosis and treatment of thyroid



cancer influence the lives of the survivors and impacts on the health-related quality of life.

David Taieb et al. [13] from France studied the determinants of medium-term quality of life in thyroid cancer patients following radioiodine ablation; 83 patients were eligible for the evaluation with Functional Assessment of Chronic Illness & Therapy (FACIT) at the time of inclusion and after 9 months post RAI. Analysis showed interesting results: high quality of life levels were associated with <45 years old men, partner and rh-TSH stimulation, but the conclusion was that the use of radioiodine ablation does not affect the medium-term quality of life scores in thyroid cancer patients.

A group from China, Hong-Xia Wu et al. [14], published in *Neuropsychiatric Disease and Treatment* an interesting study regarding the effects of psychological and behavioral interventions on health-related quality of life and mental health among DTC patients treated with post-surgical RAI. 60 patients were enrolled and the measurement instruments involved were the quality of life care questionnaire, self-rating depression scale and self-rated anxiety score. The conclusion was that psychological and behavioral interventions for patients with DTC undergoing RAI facilitated positive outcomes and the nursing care models may be a complementary strategy in these patients.

There are some studies in the literature that target patients with certainly defined demographic characteristics, involving large groups from the whole country. We selected the most relevant three studies below.

Torquil Watt et al. [15] published in 2010 a novel thyroid questionnaire for thyroid patients (ThyPRO) which can be applied in clinical practice, after it had been validated in a cross sectional study of 904 patients from Denmark.

The validation of the Korean version of the thyroid-specific quality of life questionnaire was made through a study conducted by Youjin Jeong et al. [16] from Seoul, Korea. The data were obtained from 227 patients with thyroid cancer and the reliability of the questionnaire was assessed by the Pearson correlation coefficient and by the Cronbach alpha coefficient. After the validation, the Korean physicians are free to use the questionnaire for the health-related quality of life in thyroid cancer patients.

Another study published in 2010 in *Health and Quality of Life Outcomes* by Ji in Lee [17] compared the health-related quality of life (HRQOL) of the disease free survivors of DTC from Korea with a big control group (1000 people) and the result was that the DTC free survivors experienced a significant decreased HRQOL compared with the control group. The authors used EORTC QLQ-30, BFI and HADS as measurement instruments.

Melanie Metallo et al. [18] focused on long-term quality of life and pregnancy outcomes of differentiated thyroid cancer survivors treated by total thyroidectomy and iodine during adolescence and young adult period. 45

patients were able to respond on this survey and a cross-sectional analysis was conducted using SF-36 and ISP-25. No congenital malformations or first year mortality was noted and the HRQOL of young females was not affected.

A longitudinal study was published in 2011 by Massimo Giusti et al. [19] including 128 patients followed between 2004-2008. The group control had 219 patients with surgery for benign thyroid pathology. The study confirms the wide variation of the illness perception in DTC patients and this is unrelated to the favorable clinical outcome. A special attention should be dedicated to the older patients with DTC and to those with advanced staging at the diagnosis.

Monica Vega-Vasquez et al. [20] from Puerto Rico investigated the quality of life in 75 subjects with the Spanish-version of the University of Washington Quality of Life Questionnaire. The cohort study reported a minimal overall effect on the QoL but with the future need to analyze closely and repeatedly a structured evaluation during follow-up.

The last category of this integrative literature review is based on psychosomatic interventions and behavioral help to improve the quality of life in thyroid cancer patients.

Exercise seems to play an important role in DTC patients and to minimize the treatment effect on quality of life, said Patricia dos Santos Vigarito et al. [5] in a study published in 2013. The exercise program consisted of 60 minutes of aerobic and stretching exercises, twice a week during twelve weeks.

A recent study published in the *European Journal of Nuclear Medicine and Molecular Imaging* regarding the persistent quality of life impairments in DTC patients was conducted by Eva-Maria Gamper et al. [6] The main idea of this study was the evaluation of HRQOL of the radioiodine-naïve DTC patients in comparison with the general population. 439 thyroid cancer patients were studied during 2005-2013 and the QOL was measured through the EORTC Quality of Life Questionnaire Core-30. The fatigue and the role functioning never reached the scores from the general population. In order to improve the HRQOL in DTC patients a team work with support and disease experience is needed.

The last study analyzed is actually a “point of view” from different categories involved in the management of thyroid cancer: physician, patient and psychologist [7]. The physician should not give positive diagnosis too readily even if the statistics are in favor of the good news and it is crucial for the doctors to realize that an informed patient tolerates much more than an uninformed patient. The psychologist noted that the patients are willing to provide information on different aspects of their lives. Patients can be told what other patients have perceived according to the disease. The patient’s view comes from dr. Heying Duan which is a nuclear medicine expert and a thyroid cancer patient. She noted that it is very difficult for patients to

differentiate in HRQOL between disease-related QOL issues and other general stresses. The future research must be focused on the thyroid cancer patient needs. It would be helpful for the physician to have a little training on psycho-oncology and psychological counseling support.

### Discussion

Thyroid cancer treatment management involves 3 important steps to follow: surgery, radioiodine ablation according to the guidelines, and hormone treatment with TSH suppression. The medical circuit of the patient for the management of thyroid cancer includes several physicians and some very important steps for reaching the disease-free status.

The general practitioner and the endocrinologist are the doctors who introduce the patient to the long “journey” of curing the cancer. Once the clinical diagnosis is established, the patient must be seen by the surgeon. Usually this is the most terrifying moment for the patient, the idea of being on the table with the neck dissection, fearing death. If this moment is not well-handled enough by the surgeon the long ride from now on will be very difficult. The impact of the total thyroidectomy, the idea of what is still going to happen and the long follow-up with a life-long treatment has a devastating effect on the patient. Some studies cited in the present work [8][9] analyzed the impact of the thyroidectomy and the scar from the neck dissection on the quality of life in thyroid cancer patients, emphasizing that trying to do less harm with the best medical and physical results is the best approach. The physical aspect, mostly for the female group, is even most important than the idea of having cancer. Regarding this subject, it would be interesting to study to which point does the level of life quality decrease from the moment of suspected disease and after the surgical act of thyroidectomy.

After the surgery the patients must be redirected to the multidisciplinary team (nuclear medicine/ endo-oncologist) for the post-surgical correct evaluation and for the next step in the therapy strategy. The current guidelines ( NCCN v2 2014 [21], BTA 2014 [22], ATA 2015 [23]) indicate that the most appropriate moment to perform the evaluation is between 4-6 weeks following the surgical operation and in the absence of any thyroid hormone substitute. The long withdrawal period has a very well known explanation but the absence of the thyroid hormone from the patient’s body influences the entire metabolism and the good functioning of the mental status. Therefore, the quality of life in this moment tends to decrease a lot even more when the final diagnosis (after the histopathological result) is well explained to the patient. The hypothyroidism symptoms including fatigue, weakness, weight gain, muscle cramps, constipation, irritability, memory loss and abnormal menstrual cycles in young female are translated in low scores regarding quality of life. The paper from Nygaard et al. studied the effect of using the rh-TSH instead of stopping the thyroid hormone medicine for the correct

evaluation. The study was designed as a case-control type between using rh-TSH or thyroid hormone withdrawal. As we all expected, the rh-TSH group showed better results and a better quality of life compared to the thyroid hormone withdrawal group. We all want to have the freedom and the financial status to offer our patients the best approach but maybe the big disadvantage is the high price of the rh-TSH. There are some clinical situations in which the physician is forced to use this method, but around the world it is not everyday practice.

Last but not least, the management of the thyroid cancer patient includes the moment of radiotherapy ablation for the cases where this is indicated. At this point, patients accumulate a lot of stress, even more because they think that everything will happen as in a “nuclear plant”. It is a good point to start from zero with the information regarding the real procedure and the real information on radioprotection issues. Revising the literature, we did not find any study related to the quality of life in DTC patients according to the radioprotection measures that must be followed once the patient is discharged. We think it’s a good option for future research and maybe interesting results will come.

### Conclusion

There is a growing interest in the last years for the quality of life studies, especially in the oncological field. Thyroid cancer, due to its high survival rate and long term follow-up, needs special consideration regarding this issue. Thus, supplementary strategies must be developed in order to improve the relationship between the patient and the physician.

As doctors, we must understand the emotional impact of the cancer diagnosis on the patient and we must collaborate in order to help the patient restore the psychosomatic balance and to recover the quality of life.

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