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ORIGINAL RESEARCH

Risk Factors of Deterioration in Quality of Life Scores in Thyroid Cancer Patients After Thyroidectomy

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Jie Li 
Ling Bo Xue
Xiao Yi Gong
Yan Fang Yang
Bu Yong Zhang
Jian Jin
Qing Feng Shi
Yong Hong Liu 

Thyroid and Breast Surgery, Cangzhou Central Hospital, Cangzhou City 061000, People's Republic of China

Objective: Despite the expectation of normal life expectancy for thyroid cancer, there are concerns about the decreased quality of life (QoL). The present study investigated the potential risk factors of deterioration in QoL scores in thyroid cancer patients after thyroidectomy.

Materials and methods: A total of 286 patients who were diagnosed with thyroid cancer after thyroidectomy were involved in this prospective, single-center, observational study from November 2018 to June 2019. The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 was used to assess the QoL 3 months after thyroidectomy. We investigated the effects of demographics (age, gender, education, marital status, area of residence, and annual mean income), tumor characteristics (histology, clinical stage, presence of metastasis, surgery type, and radiotherapy), and neurological deficits induced by recurrent nerve or superior laryngeal injury on QoL.

Results: The mean overall QoL in thyroid cancer survivors was 65.93 ± 9.00 (on a scale of 0–100, where 100 was the best). Multivariate regression analysis confirmed that clinical stage ($P < 0.010$), surgery type ($P < 0.001$), histology ($P < 0.001$), neurological deficits ($P < 0.001$), and marital status ($P < 0.001$) were independent risk factors for decreased QoL 3 months after thyroidectomy.

Conclusion: Our study indicated that clinical stage, surgery type, histology, neurological deficits, and marital status were independent risk factors for decreased QoL at 3 months after thyroidectomy. Further exploration and validation of these findings in larger prospective studies are warranted.

Keywords: quality of life, thyroid cancer, thyroidectomy

Introduction

The incidence of thyroid cancer has been increasing in China and in several parts of the world, and this increase is predominant among differentiated thyroid cancers, which are characterized by good outcomes. The average life expectancy of thyroid cancer patients is similar to that of the general population.^{1,2} Quality of life (QoL) is a subjective clinical endpoint that has become increasingly important in health outcomes research, particularly in cancer clinical trials, over the past two decades.³ Therefore, the current thyroid cancer guidelines for patient care are shifting toward the decrease in morbidity and increase in QoL from merely increasing the survival rate.⁴

Previous studies reported that thyroid cancer survivors have impairments in health-related QoL.^{5–8} More surprisingly, the QoL in thyroid cancer patients is at

Correspondence: Yong Hong Liu
Thyroid and Breast Surgery, Cangzhou Central Hospital, No. 16 Xinhua Road, Yunhe Qu, Cangzhou City 061000, People's Republic of China
Tel +86-15733758110
Fax +86 317-207-2692
Email lyh15733758110@hotmail.com

the same level as that in patients with more aggressive cancers.⁹ The assessment and identification of risk factors of decreased QoL in thyroid cancer survivors provide insights into their experiences of the disease and might support the choice and design of appropriate interventions and survivorship care plans. Thus, in this prospective, single-center, observational study, we investigated the potential risk factors of QoL deterioration in thyroid cancer patients undergoing thyroidectomy.

Materials and Methods

This study was conducted in accordance with Helsinki declaration and approved by the ethics committee of Cangzhou Central Hospital (No. 2017-081-01). All eligible participants were familiarized in advance with the study, its objectives and methods, the confidentiality of data, and the possibility of withdrawing from the study at any time. These participants also provided a written consent to participate in the study.

Study Population

After receiving Institutional Review and Ethics Board approval, patients that were recently diagnosed with thyroid cancer and underwent thyroidectomy were involved in this prospective, single-center, observational study from November 2018 to June 2019. The inclusion criteria were as follows: age ≥ 18 years at diagnosis; primary thyroid cancer diagnosis with clinicopathological information and undergoing thyroidectomy; informed about the aim of the study; and volunteered to participate. The exclusion criteria were as follows: language barriers, severe cognitive impairment, mental diseases, far geographical distance, presence of other primary tumors, refusal to participate, and incapable of independently filling out the questionnaires.

Evaluation Tools of QoL

Face-to-face semi-structured interviews were offered either to coincide with a future hospital appointment or at the patient's home at a time that is convenient for them. QoL was assessed using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30), which was originally proposed by Aaronson et al.¹⁰ The QLQ-C30 includes 30 items and measures 5 functional scales (i.e., physical, role, emotional, cognitive, and social functioning), global health status, financial difficulties, and 8 symptom scales (i.e., fatigue, nausea and vomiting, pain,

dyspnea, insomnia, appetite loss, constipation, and diarrhea).¹¹ A summary score was calculated from 13 scales (excluding global QoL and financial difficulties), with the symptom scales being reversed (100-symptom scale) to obtain a uniform direction of all scales,^{12,13} as follows: QLQ-C30 summary score = (physical functioning + role functioning + social functioning + emotional functioning + cognitive functioning + [100 – fatigue] + [100 – pain] + [100 – nausea/vomiting] + [100 – dyspnea] + [100 – insomnia] + [100 – appetite loss] + [100 – constipation] + [100 – diarrhea])/13.

Predictive Factors Affecting QoL

To identify factors at diagnosis that were predictive of QoL measured with EORTC QLQ-C30 at 3 months of follow-up, we investigated the effects of the following factors: age, gender, education, marital status, area of residence, and annual mean income. We also collected tumor characteristics, including histology (papillary, follicular, medullary, and undifferentiated), clinical stage, presence of metastasis, surgery type and radiotherapy. The extent of surgery was categorized as total thyroidectomy (total, subtotal, and near total) and lobectomy (partial lobectomy, lobectomy, and/or isthmusectomy). In addition, neurological deficits induced by recurrent nerve or superior laryngeal injury were collected.

Sample Size

The final model tested consisted of 13 dimensions,¹² which resulted in an initial estimate of 260 individuals. However, we added a loss rate of 20%, thereby increasing the minimum sample size to 286 individuals.

Statistical Analyses

Statistical analyses were performed using SPSS version 13.0 (SPSS Inc., Chicago, IL). Multivariate regression analyses were used to assess the associations of demographic and tumor characteristics with decreased QoL. A two-tailed $P < 0.05$ was considered statistically significant.

Results

Among the 298 patients that were recently diagnosed with thyroid cancer after thyroidectomy, 5 patients refused to participate, 2 patients emigrated to other cities, 2 patients had mental disease, 3 patients could not independently fill out the questionnaires, and 286 patients were ultimately involved in this study.

Table 1 Demographic and Tumor Characteristics of 286 Participants (n, %)

Demographic Characteristics	(n, %)	Tumor Characteristics	(n, %)
Gender		Histology	
Male	60 (21.0%)	Papillary	258 (90.2%)
Female	226 (79.0%)	Follicular	24 (8.4%)
Age (year)		Medullary	4 (1.4%)
≤60	238 (83.2%)	Clinical stage (AJCC8)	
>60	48 (16.8%)	I	237 (82.8%)
Education		II	42 (14.7%)
Low (<12 years)	239 (83.6%)	III	6 (2.1%)
High (≥12 years)	47 (16.4%)	IV	1 (0.4%)
Marital status		Presence of metastasis	
Married	232 (82.9%)	Yes	1 (0.4%)
Unmarried/divorced	49 (17.1%)	No	285 (99.6%)
Area of residence		Surgery type	
City	87 (30.4%)	Lobectomy	194 (67.8%)
Rural or regional	199 (69.6%)	Total thyroidectomy	92 (32.2%)
Annual mean income		Radiotherapy	
Low	76 (26.6%)	Yes	19 (6.6%)
Middle	155 (54.2%)	No	267 (93.4%)
High	55 (19.2%)	Neurological deficits	
		Yes	11 (3.8%)
		No	275 (96.2%)

Abbreviation: AJCC8, The 8th Edition of the American Joint Committee on Cancer.

The general information of demographic and tumor characteristics is shown in **Table 1**. Overall, the majority of the participants was female (79.0%), aged ≤60 years old (83.2%), had low educational attainment (83.6%), married (82.9%), lived in rural or regional areas (69.6%), and had middle mean income (54.2%). Approximately 90.2% of patients had papillary cancer, 82.8% were clinical stage I, 0.4% had metastasis, 67.8% had undergone lobectomy, and 6.6% were undergoing radiotherapy. Of the patients, 3.8% had neurological deficits induced by recurrent nerve or superior laryngeal injury.

Multivariate regression analysis confirmed that clinical stage ($P < 0.001$), surgery type ($P < 0.001$), histology ($P < 0.001$), neurological deficits ($P < 0.001$), and marital status ($P < 0.001$) were independent risk factors for decreased QoL 3 months after thyroidectomy (**Table 2**). Further analysis (**Table 3**) showed that clinical stage I, lobectomy, papillary, non-neurological deficits, and marital status were related to the QoL score.

Discussion

The concept of QoL is relatively new and has acquired growing importance in recent decades. Particular attention should be given to the QoL of patients, especially in the presence of risk factors impairing QoL. Although

differentiated thyroid cancer is perceived as a “good cancer,” cancer-related decreased QoL is still common for disease-free thyroid cancer survivors.^{14–19} The results of our study indicated decreased QoL in thyroid cancer survivors and that marital status, histology, clinical stage, and surgery type were independent risk factors for decreased QoL 3 months after thyroidectomy.

The reasons for decreased QoL remain largely unexplained, but several studies reported the possible reasons. Some authors have attributed decreased QoL to cancer-related fatigue, which is a symptom that is frequently experienced by survivors regardless of tumor type or its treatment and not likely to be relieved by rest.^{20,21} Another possible explanation for decreased QoL is because replacement therapy with levothyroxine cannot normalize T4 and T3 concentrations in all tissues,^{22–24} which might play a role in persisting symptoms and decreased QoL among hypothyroid cancer patients. Emotional and psychological concerns are also largely unmet in thyroid cancer survivors.^{25–27}

A previous observational cross-sectional study showed that the factors influencing QoL are TNM stage, radioiodine therapy and dose, and presence of metastases.²⁸ By contrast, radiotherapy and presence of metastasis were not independent risk factors for decreased QoL at 3 months

Table 2 Logistic Regression Analyses of Factors Associated with Decreased QoL

	B Coefficient	Standard Error	P value	Beta	95% Confidence Interval for B
Clinical stage	-10.569	0.729	<0.001	-0.555	-12.003 -- -9.135
Surgery type	-4.179	0.688	<0.001	-0.217	-5.533 -- -2.824
Histology	-6.340	0.888	<0.001	-0.252	-8.089 -- -4.591
Neurological deficits	-8.472	1.802	<0.001	-0.181	-12.019 -- -4.925
Marital status	-3.417	0.893	<0.001	-0.143	-5.176 -- -1.659

Abbreviation: QoL, Quality of life.

Table 3 QoL at 3 Months After Thyroidectomy on the Basis of the Risk Factors

	QoL Score	P
Clinical stage (AJCC8)		
I	70.60 (7.73)	<0.001
II	54.62 (12.31)	
III and IV	38.12 (5.64)	
Surgery type		<0.001
Lobectomy	70.60 (6.92)	
Total thyroidectomy	66.16 (15.55)	
Histology		<0.001
Papillary	70.41 (7.04)	
Follicular and Medullary	55.41 (13.84)	
Neurological deficits		<0.001
Yes	45.77 (6.75)	
No	70.09 (8.16)	
Marital status		<0.001
Married	70.60 (5.75)	
Unmarried/divorced	57.91 (13.17)	

Note: Continuous variables are presented as median (interquartile range) due to abnormal distribution.

Abbreviations: QoL, Quality of life; AJCC8, The 8th Edition of the American Joint Committee on Cancer.

after thyroidectomy in our study. We speculated that the discrepancy might be related to low incidence, with 0.4% of patients with metastasis and 6.6% undergoing radiotherapy. Consistent with previous report, marital status was also associated with low QoL scores, indicating that family support is considerably important to thyroid cancer survivors.²⁹ Patients do not know what kind of symptoms they may be facing and are often left alone with their diagnosis and fears. Family, particularly the patient's spouse, is central to all aspects of social support, including emotional, instrumental, and informational support.

The introduction of advances in diagnostic methods combined with increased medical surveillance and access to health care services led to the overdiagnosis of thyroid cancer,^{30,31} which may have never caused symptoms or harm if

undetected.^{32,33} In addition, the majority of patients who were diagnosed with thyroid cancer underwent total thyroidectomy. In a previous study, Nickel et al reported that overdiagnosis leads to physical and psychological burdens, which are more prevalent among patients who have total thyroidectomy than those who have hemithyroidectomy.³⁰ Moreover, Conzo et al³⁴ reported that hemithyroidectomy may avoid adverse effects, such as recurrent laryngeal nerve paralysis and permanent hypoparathyroidism, and lead to low mean hospitalization stays and costs. Considering low-risk follicular neoplasm solitary lesions, hemithyroidectomy remains the safest standard.³⁴ In case of multiglandular disease or highly malignant tumor, which might be associated with a high risk of cancer, total thyroidectomy is recommended.³⁵

This study had several potential limitations. First, the duration might not have been sufficiently long. Studies with longer follow-up durations are needed to determine the long-term effects of factors on the QoL in these patients. Second, endocrine function includes T4 therapy, and the levels of T4 suppression need to be evaluated. Third, the data were collected from a single center, and the sample was relatively small. Fourth, the cohort of study participants might not entirely reflect the Chinese population; that is, our sample lacks the diversity of race/ethnicity.

In conclusion, the results of our study indicated that marital status, histology, clinical stage, and surgery type were independent risk factors for decreased QoL 3 months after thyroidectomy. Future studies are needed to investigate these factors in depth, possibly allowing health resources to be allocated to support patients with thyroid cancer.

Abbreviation

QoL, Quality of life.

Disclosure

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