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Quality of Life of Survivors of Thyroid Cancer Is Not Inferior to That in Subjects without Cancer: Long-Term after Over 5 Years

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Background: Patients with thyroid cancer undergo less extensive surgery and additional therapies compared to those with other cancers. We aimed to compare the quality of life (QoL) between patients with thyroid cancer and healthy subjects using representative data from Korea. Differences in QoL of thyroid cancer survivors according to the duration after cancer diagnosis was also evaluated.

Methods: This population-based cohort study included 50,278 subjects who participated in the Korea National Health and Nutrition Examination Survey between 2007 and 2017. QoL was compared between patients with thyroid cancer and healthy subjects using self-reported data from the EuroQoL (EQ)-5 dimension (5D) and EQ-visual analog scale (VAS). Propensity score matching was used to match thyroid cancer survivors to healthy subjects (1:5 matching).

Results: Linear regression with univariate analysis showed that the presence of thyroid cancer was positively correlated with better EQ-5D index scores (β-coefficient=0.010, P=0.046). After adjusting for multiple covariables, statistical significance was maintained. EQ-VAS fails to demonstrate any significant correlation. Among the EQ-5D categories, patients with thyroid cancer showed better self-care than healthy subjects. Thyroid cancer duration did not correlate with the EQ-5D index score. In subgroup analyses, compared to patients with thyroid cancer duration of <5 years, no significant difference was observed in the correlation between the EQ-5D index score and survival duration in those with thyroid cancer duration of 5 to 9 years and ≥10 years.

Conclusion: Using a large-scale nationwide population-based database, our study demonstrated better QoL, especially in terms of self-care, among thyroid cancer survivors than among healthy subjects without cancer.

Keywords: Thyroid neoplasms; Health status; Quality of life

INTRODUCTION

Owing to the development of early detection tools and various cancer treatment modalities, the detection rate of thyroid cancer has tremendous increased [1,2]. In Korea, thyroid cancer is commonly diagnosed at young age (age 40s), with a favorable 5-year relative survival rate of approximately 90% to 100% [3]. Generally, total thyroidectomy or lobectomy is the first-line

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treatment for patients with thyroid cancer. After surgical removal, all patients who undergo total thyroidectomy and some who undergo lobectomy require levothyroxine (T4) replacement. Patients with a high risk of recurrence receive a high dose of T4 to suppress and maintain thyrotropin (TSH) levels below the lower normal range, that is, exogenous subclinical hyperthyroidism, to prevent recurrence for a certain period [4]. Patients with a low-to-intermediate risk receive a relatively lower T4 dose to maintain TSH levels in lower normal range. Nearly 50% patients undergo total thyroidectomy, followed by radioactive iodine (RAI) ablation according to the risk of recurrence [1], and a subsequent iodine scan would be required during cancer surveillance. RAI therapy and iodine scans require a low-iodine diet, which is uncommon in Korea. In patients undergoing thyroid hormone withdrawal for TSH stimulation before RAI, iatrogenic overt hypothyroidism can cause generalized edema and general weakness. In addition to surgery and surgery-related complications, patients with thyroid cancer can experience inconvenience (taking medicine) and an iatrogenic pathologic state (subclinical hyperthyroidism or overt hypothyroidism) due to the effects of thyroid cancer treatment and follow-up strategies. Thus, unfavorable health outcomes due to primary cancer treatment have received much attention [5]. In addition, outcomes such as cardiovascular disease [6]; osteoporosis [7]; and metabolic syndrome, including insulin resistance, obesity, and hypertension [8] are commonly observed after surgical therapy, followed by RAI or TSH suppression. Given the relatively young age at diagnosis and high survival rate among patients with thyroid cancer, quality of life (QoL) and long-term adverse health outcomes are of interest to many physicians. Generally, cancer survivors experience physical and mental difficulties after cancer treatment. Therefore, it is reasonable to suspect that QoL in cancer survivors may be poorer than that in subjects without cancer.

Previous studies have reported that thyroid cancer survivors experience physical or psychological distress [9-14]. These studies had small sample sizes and short-term follow-up period [10,11,13] or lacked a healthy control group [9-12,15]. These studies also lacked valid tools to evaluate health-related (HR) QoL [9-11]. Moreover, limited studies have evaluated long-term HRQoL in a large sample of thyroid cancer survivors. Thus, we aimed to investigate HRQoL using validated questionnaires in thyroid cancer survivors and compared it to that in healthy subjects to better tailor support for thyroid cancer survivors with high survival rates.

METHODS

Study population and data collection

This population-based cohort study used data of the Korea National Health and Nutrition Examination Survey (KNHANES) from KNHANES IV to VII (2007 to 2017). The KNHANES conducted by Korean Centers for Disease Control and Prevention for Health Statistics is an independent dataset obtained from the general South Korean population. The selection of participants for the survey is based on a stratified multistage probability sampling design for the South Korean population and a two-stage stratified systematic sampling method. The KNHANES monitors the health and nutritional status of the Korean population, and assessments are conducted by trained interviewers. The details of the database are described elsewhere (https://knhanes.cdc.go.kr). This study complied with the ethical standards of the Declaration of Helsinki and was approved by the Catholic University of Korea, Catholic Medical Center, Eunpyeong St. Mary's Hospital Institutional Review Board (IRB approval No. PC20ZASI0091). The requirement for written informed consent was waived due to the use of previously collected and anonymized data. Among the 89,630 subjects who participated from KNHANES IV to KNHANES VII, 38,285 subjects were excluded based on the following criteria: age <19 years (n=20,691), self-reported history of chronic renal disease (n=261), cerebrovascular disease (n=1,369), rheumatic or osteoarthritis (n=8,846), moderate depression (n=678), or other cancers except thyroid cancer (n=15), and missing data on EuroQoL (EQ)-5 dimension (5D) utility scores (n=27,389). In this study, data from 50,278 participants were analyzed. To increase sensitivity, reduce sampling bias, and overcome confounding and selection bias when utilizing large and representative datasets, sampling weights were adjusted according to demographic factors. Propensity score matching (PSM) was performed between 312 thyroid cancer survivors and 49,966 healthy subjects from 50,278 participants from 2007 to 2017. We used the following algorithms for forming matched pairs of thyroid cancer survivors and healthy subjects: optimal matching and greedy nearest neighbor matching within specified caliper widths (0.25). Covariates for PSM matching were sex, age, smoking status, drinking behavior, marital status, education level, income level, physical activity, and self-perceived stress. After PSM matching, 183 subjects with thyroid cancer and 915 subjects without any cancer were extracted. Finally, a total of 1,098 subjects were analyzed in this study. The propensity score for thyroid cancer probability was estimated using a multivariate logis-

tic regression model. The greedy nearest neighbor algorithm was used to match thyroid cancer survivors to five healthy subjects (1:5 matching). After matching, the standardized mean differences (SD) were calculated to verify the quality of matching; if the SD was <10%, matching was confirmed as the best balance between the two groups.

Demographic variables and lifestyle factors

Demographic and lifestyle variables of the subjects were collected using a questionnaire. The following variables were assessed: sex, age, smoking status (stratified into current smokers and non-smokers, including ex-smokers), drinking behavior (classified as non-to-moderate drinking and risky drinking; >30 g/day of alcohol), marital status (married or separated; categorical), educational status (divided into two groups—less than middle school and greater than middle school), income level (categorized into two groups—low/mid-low and mid-high/high), physical activity (defined as activity consisting of at least 30 minutes of walking for at least 5 days a week), and self-perceived stress according to the response (yes or no; categorical).

Sub-classification by duration of thyroid cancer

Follow-up and management strategies for patients with thyroid cancer, including T4 dosing and modality or frequency of laboratory/imaging studies, are subject to change over time (dynamic or ongoing risk stratification) [16]. Thus, the QoL of thyroid cancer survivors can differ according to the time interval after disease diagnosis. According to American and Korean Thyroid Association guidelines, additional treatment and surveillance tools beyond thyroid ultrasonography (US) are rarely indicated if there is no suspected remnant disease or recurrent disease in over 10 years [4,17]. Therefore, we categorized thyroid cancer survivors into groups based on time of diagnosis—<5, 5–9, and ≥10 years after diagnosis.

Assessment of QoL

HRQoL was assessed using the Korean version of the EQ-5D, which has been included to evaluate QoL in the questionnaire since 2005 (KNHANES III) [18]. The EQ-visual analog scale (VAS) score was also measured in the KNHANES from 2007 to 2012. The EQ-5D comprises five targeted questions—mobility, self-care, usual activities, pain/discomfort, and anxiety/depression—to represent the current health status, EQ-5D score, and EQ-VAS score [19]. Each dimension is scored using three severity levels (no problem, some problems, and severe problems). Population-specific value sets are used for comparisons across different populations. The EQ-5D index is a continuous value that ranges from −0.171 (indicating poorer health status) to 1 (indicating the best health status) [20]. The EQ-VAS derives information from the perception of subjective health status, scored on a VAS with endpoints labeled "the best health you can imagine" and "the worst health you can imagine." The EQ-VAS comprises a scale ranging from 0 (worst health status) to 100 (best health status). The detail of questionnaire of HRQoL were shown in section of Supplemental Methods with Supplemental Table S1.

Statistical analysis

Statistical analysis was performed to reflect the complex sampling design and sampling weights of KNHANES to provide nationally representative prevalence estimates. The SSAS® PROC SURVEY module was used to consider strata, clusters, and weights. Demographic variables including sex, smoking status, drinking behavior, marital status, educational status, income levels, physical activity, and self-perceived stress were analyzed by a complex sample analysis using Pearson's chi-square test. The characteristics of each group were compared using independent *t* tests for continuous variables. Based on the data characteristics, the results are expressed as mean±standard error (SE), geometric means (95% confidence interval), or percentages, as appropriate. Adjusted linear regression analysis was performed to test for significant differences in the EQ-5Q score. To determine the association between thyroid cancer and EQ-5D scores, complex sample logistic regression analysis was performed. All statistical analyses were performed using SAS software version 9.4. (SAS Institute Inc., Cary, NC, USA). A *P* value of <0.005 was considered statistically significant.

RESULTS

Baseline characteristics between patients with thyroid cancer and healthy subjects

Table 1 shows baseline characteristics between thyroid cancer survivors and healthy subjects before and after 1:5 PSM matching. Before matching, there were differences in sex, age, behavior, and education level between thyroid cancer survivors and healthy subjects. Data on 183 thyroid cancer survivors and 915 healthy subjects were analyzed. The mean age of thyroid cancer survivors was 51.2±0.9 years, and 76.4% patients were women. Smoking status, drinking habit, marital status, education status, income levels, and physical activity were similar between the groups after PSM matching. Absence of self-perceived

Table 1. A comparison of Baseline Characteristics between Subject with Thyroid Cancer and Control

Clinical parameters	Before 1:5 matching		*P* value	After 1:5 matching		*P* value
	Thyroid cancer (*n*=312)	Non-cancer (*n*=49,966)		Thyroid cancer (*n*=183)	Non-cancer (*n*=915)	
Sex			<0.001			1.000
Male	53 (17.0)	233,229 (46.5)		43 (23.5)	215 (23.5)	
Female	140 (83.0)	700 (76.5)		140 (83.0)	700 (76.5)	
Age, yr	53.4±12.0	51.1±12.0	<0.001	51.2±11.0	51.1±12.0	0.8885
Smoking status			<0.001			0.9746
Current smoker	52 (16.7)	20,086 (40..4)		43 (23.5)	216 (23.6)	
Non-smoker	260 (83.3)	29,689 (59.6)		140 (76.5)	699 (46.4)	
Risky drinking	11 (5.7)	6,080 (16.2)	<0.001	10 (5.5)	57 (6.2)	0.6931
Marital status			0.4755			0.5376
Yes	253 (86.5)	36,142 (87.9)		158 (86.3)	805 (88.0)	
No	40 (13.5)	5,000 (12.1)		25 (13.7)	110 (12.0)	
Education status			0.0265			0.8737
Less than middle school	99 (31.8)	13,104 (26.3)		44 (24.0)	215 (23.5)	
Greater than middle school	212 (68.2)	36,768 (73.7)		139 (76.0)	700 (76.5)	
Income			0.0757			0.9066
Low to mid low	110 (365.7)	20,116 (40.7)		55 (30.1)	279 (30.5)	
Mid high to high	198 (64.3)	28,308 (59.3)		128 (69.9)	636 (59.5)	
Physical activity			0.4398			0.9784
Yes	134 (43.0)	20,282 (40.8)		83 (45.4)	414 (45.3)	
No	178 (57.0)	29,438 (59.2)		100 (54.6)	501 (54.7)	
Self-perceived stress			0.0537			0.2865
Yes	66 (21.2)	12,922 (25.9)		37 (20.2)	155 (16.9)	
No	246 (78.8)	36,865 (74.1)		146 (79.8)	760 (83.1)	

Values are expressed as number (%) or mean±standard error.

stress did not differ between the groups. The unadjusted mean EQ-5D index score was 1.0±0.0 in both groups (*P*=0.057). No difference in EQ-VAS scores was observed between thyroid cancer survivors and healthy subjects (74.9±2.5 vs. 76.5±1.0, *P*=0.503). Thus, the weighted and matched variables were not significantly different between the groups.

Frequencies of reporting problems according to EQ-5D categories in patients with thyroid cancer and healthy subjects using the weighted and matched model

The proportion of subjects who reported problems in the five categories of the EQ was analyzed (Table 2). The percentage of participants who answered "mild-to-severe problem" for the mobility, self-care, and usual activity; "none" for pain/discomfort; and "none" for anxiety/depression dimensions of the EQ-5D was similar between the groups. None of the thyroid cancer survivors responded to the "mild-to-severe problem" in terms of self-care.

Multivariate linear regression model for EQ-5D score and EQ-5D index in patients with thyroid cancer versus healthy subjects

In linear regression, the presence of thyroid cancer was positively correlated with a better EQ-5D index score (β coefficient=0.010, *P*=0.0460). Though EQ-VAS showed negative correlation, no statistical significance was observed, (β coefficient=–1.670, *P*=0.4636) (Table 3). After adjustment for age; sex; income level; education level; marital status; and lifestyle habits including smoking, risky drinking, and physical activity, an increase in the EQ-5D index score in patients with thyroid cancer was observed compared to that in healthy subjects (β coefficient=0.010, *P*=0.046). Among the factors comprising the

Table 2. Distribution of Reporting Problems according to EQ-5D Categories in Thyroid Cancer Survivor and Non-Cancer Group

EQ-5D	Thyroid cancer (*n*=183)	Non-cancer (*n*=915)	*P* value
EQ-5D_Mobility			0.1034
No problem	174 (97.0)	848 (94.0)	
Mild-to-severe problem	9 (3.0)	67 (6.0)	
EQ-5D_Self-care			NA
No problem	183 (100.0)	904 (98.9)	
Mild-to-severe problem	0	11 (1.1)	
EQ-5D_Usual activity			0.4610
No problem	175 (95.5)	878 (96.7)	
Mild-to-severe problem	8 (4.5)	37 (3.3)	
EQ-5D_Pain/Discomfort			0.7330
None	156 (84.2)	751 (82.9)	
Mild to severe	27 (15.8)	164 (17.1)	
EQ-5D_Anxiety/Depression			0.4971
None	171 (94.3)	846 (92.7)	
Mild to severe	12 (5.7)	69 (7.3)	

Values are expressed as number (%). Weighted and matched (1:5) sample.
EQ-5D, EuroQoL-5 dimension; NA, not available.

EQ-5D index, thyroid cancer survivors showed a lower risk of having problems with self-care.

Correlation between EQ-5D index score and thyroid cancer duration

The EQ-5D index score was negatively correlated with thyroid cancer duration. However, this difference was not significant (β coefficient=–0.001, *P*=0.2887). Considering the different treatment and follow-up strategies based on the thyroid cancer duration, we performed subgroup analysis according to the thyroid cancer duration in thyroid cancer survivors. The thyroid cancer duration in 40,292, 38,251, and 16,981 patients was <5 years (mean, 2.8±1.0 years), 5–9 years (mean, 6.4±1.3 years), and >10 years (mean, 13.9±4.1 years), respectively. The EQ-5D index score showed a positive correlation for the duration of 5–9 years (β coefficient=0.003, *P*=0.008). It decreased in thyroid cancer survivors with a disease duration of >10 years (β coefficient=–0.026, *P*=0.168), although the association was not significant (Table 4).

DISCUSSION

In the analysis of a nationwide population-based database, the QoL of thyroid cancer survivors, estimated by the EQ-5D index score, was non-inferior to that of healthy subjects without any cancer. The QoL of thyroid cancer survivors showed even better scores due to the increased self-care index compared to non-cancer subjects. Additionally, no difference was observed in the QoL of thyroid cancer survivors according to thyroid cancer duration.

Differentiated thyroid cancer has an excellent prognosis with a high long-term survival rate [21,22]. However, despite the favorable long-term prognosis, there have been concerns regarding HRQoL in thyroid cancer survivors arising from their unique treatment modalities. HRQoL in thyroid cancer survivors in relation with treatment modalities such as surgery including total thyroidectomy, and lobectomy, RAI therapy, and TSH suppressive therapy depending on disease stages has been established [4,17,23-25]. With respect to surgery, one study showed lower HRQoL in thyroid cancer survivors due to tightening and pain around surgical scars [26] while another study in the United States showed no impact of surgical wounds on HRQoL 2 years after surgery [27]. The differences in HRQoL among total thyroidectomy, lobectomy, and robot-associated thyroidectomy remain inconclusive [5,28-30]. The risk of sialadenitis and dysphagia after RAI, anxiety before RAI, iatrogenic hypothyroidism, and hyponatremia during a low-iodine diet with thyroid hormone withdrawal were associated with low HRQoL [11,31-33]. In contrast to thyroid hormone withdrawal, preparation for RAI therapy with recombinant TSH was positively correlated with HRQoL [5,34,35]. HRQoL negatively correlated with TSH suppression [10,36-39]. In addition to the total HRQoL, chronic subclinical hyperthyroidism or hyperthyroidism can cause medical problems such as cardiovascular complications [6], bone disease [7], muscle dysfunction [40], and metabolic disease [8].

Most studies previously evaluated HRQoL according to treatment modality in only thyroid cancer survivors without comparative data and focused on depression, anxiety, fatigue, and concern about recurrence of thyroid cancer. Some articles evaluated HRQoL without valid tools or normative data [9-11,15]. After developing, validating, and translating questionnaires such as the EQ-5D [41], Thyroid Cancer Survivors' Association (ThyCA)QoL [42], Thyroid-Specific Patient Reported Outcome (ThyPRO) [43], and European Organization for Research and Treatment of Cancer (EORTC)-Quality of Life Question-

Table 3. Multivariate Linear Regression Model for EQ-5D Score and EQ-5D Index in Subjects with Thyroid Cancer Compared to Non-Cancer Group (n=183)

Parameter	β-coefficient (95% CI)	Odds ratio (95% CI)	*P* value
Crude model			
EQ-5D index score	0.010 (0.000 to 0.020)		0.046
Mobility		0.50 (0.208 to 1.176)	0.111
Self-care		<0.01 (<0.001)	<0.000
Usual activity		1.41 (0.559 to 3.578)	0.464
Pain/Discomfort		0.91 (0.530 to 1.564)	0.733
Anxiety/Depression		0.76 (0.351 to 1.666)	0.499
EQ-VAS	–1.670 (–6.558 to 3.218)		0.464
Model 1			
EQ-5D index score	0.001 (0.000–0.019)		0.051
Mobility		0.516 (0.209 to 1.274)	0.151
Self-care		<0.001 (<0.001)	<0.000
Usual activity		1.509 (0.580 to 3.924)	0.398
Pain/Discomfort		0.906 (0.527 to 1.556)	0.720
Anxiety/Depression		0.764 (0.352 to 1.660)	0.496
EQ-VAS	–1.796 (–6.642 to 3.049)		0.467
Model 2			
EQ-5D index score	0.010 (0.000 to 0.019)		0.045
Mobility		0.513 (0.203 to 1.300)	0.159
Self-care		<0.001 (<0.001)	<0.000
Usual activity		1.472 (0.557 to 3.889)	0.434
Pain/Discomfort		0.902 (0.524 to 1.553)	0.710
Anxiety/Depression		0.774 (0.355 to 1.687)	0.519
EQ-VAS	–2.099 (–7.109 to 2.911)		0.411
Model 3			
EQ-5D index score	0.001 (0.000 to 0.019)		0.046
Mobility		0.534 (0.209 to 1.367)	0.191
Self-care		<0.001 (<0.001)	<0.000
Usual activity		1.548 (0.572 to 4.189)	0.389
Pain/Discomfort		0.904 (0.523 to 1.563)	0.718
Anxiety/Depression		0.778 (0.356 to 1.701)	0.529
EQ-VAS	–1.805 (–6.637 to 3.027)		0.464

Model 1: adjusted for age and sex; Model 2: adjusted for age, sex, income level, education level, and marital status; Model 3: adjusted for age, sex, income level, education level, marital status, and lifestyle habits (smoking, risky drinking, and physical activity).
EQ-5D, EuroQoL-5 dimension; CI, confidence interval; VAS, visual analog scale.

Table 4. Association with Duration of Thyroid Cancer and EQ-5D Index Score in Thyroid Cancer Survivors

Parameters (cancer duration)	β-Coefficient (95% CI)	*P* value
<5 years (n=75)	Reference	
5–9 years (n=72)	0.003±0.008 (–0.013 to 0.019)	0.6854
≥10 years (n=36)	–0.026±0.018 (–0.062 to 0.011)	0.168

EQ-5D, EuroQoL-5 dimension; CI, confidence interval.

naire-30 (EORTC-QLQ-C30) [44], several studies have adapted these tools. A cross-sectional study (n=316) by Lee et al. [45] and a German cohort study (n=121) [46] showed that HRQoL in survivors of thyroid cancer was lower than that in the general population. Additionally, anxiety, depression, and levels of fatigue significantly determined the lower HRQoL based on the EORTC-QLQ-C30. A recent study using EQ-5D or EQ-VAS concluded that HRQoL in thyroid cancer survivors was lower

than that in the reference or general population [47]. A Chinese population-based survey using the EORTC-QLQ-C30 combined with SF-36 showed that thyroid cancer survivors had impaired HRQoL [48]. However, these studies included only subjects with relatively short duration after surgery (mean 37.3± 28.8 months [45]) or a short time since diagnosis (mean 5 years with range from 1 to 27 years [47], 2.6±3.6 years [48]) Also, subjects could not represent the population.

In terms of the duration of thyroid cancer, there are reports that impaired HRQoL is correlated with short-term follow-up (<5 years) [10,14]. HRQoL was restored to normal after 12 to 20 years of follow-up [14]. However, no significant correlation was observed between the duration of thyroid cancer and HRQoL by EQ-5D in this study. Additionally, compared to subjects with a thyroid cancer duration of less than 5 years, HRQoL was not inferior in thyroid cancer survivors with a longer duration. The different results of our study with those of previous studies might be due to the population distribution. In our study, more than half of the population (59.0%) had a disease duration >5 years.

Our study has several advantages over previous studies. First, it included a relatively large number of subjects who were representative of the nationwide population. Second, a validated tool for QoL assessment was used. Finally, there were a substantial number of long-term survivors more than 5 years after the diagnosis of the disease. Surprisingly, the EQ-5D and EQ-VAS scores were not significantly different between the thyroid cancer survivor and non-cancer control groups. One possible explanation for the similar HRQoL is the high percentage of education level (77.8%) in the study population. A lower educational level is associated with a poor HRQoL index [9,13,42]. Highly educated subjects have a better understanding of the disease and are more satisfied [49]. Another possible explanation is the marital status. Among thyroid cancer survivors, 83.4% were married and received family support [50].

To our knowledge, this is the first study to utilize data from the third to seventh editions of the KNHANES to investigate the association between thyroid cancer and health-related QoL. This study was based on a large sample size from a nationally representative database. The use of PSM to match thyroid cancer survivors to healthy individuals enhanced the reliability of our results and minimized selection bias. Thyroid cancer survivors were matched by sex, age, education, and income level to five healthy subjects (non-cancer group) to intensify comparability. However, this study had several limitations.

First, there have been the specific instruments with cross-cultural validity for evaluating HRQoL in thyroid cancer such as THYCA-QoL [42] and ThyPRO [43]. The KNHANES has used EQ-5D to assess HRQoL in general population and EQ-5D and EQ- VAS might not be the best available HRQoL for thyroid cancer patients. Thus, thyroid cancer-specific tool is necessary to evaluate the health outcome in general population. Second, the causal relationship between thyroid cancer and related QoL could not be assessed because of the cross-sectional study design. Third, underreporting could not be excluded from the self-reporting system. Fourth, we could not exclude the comorbidities such as chronic pulmonary disease and diabetes mellitus which are meaningfully associated with HRQoL due to sample size. Finally, we could not obtain information on thyroid cancer stages, histology of thyroid cancer, and types of thyroid cancer treatment (T4 dose, extent of surgery, additional post-operative medications, and RAI therapy) because the KNHANES data lack specific clinical features. Therefore, the factors affecting HRQoL could not be identified. The combination of representative and clinical data could provide an excellent result for QoL in thyroid cancer survivors according to multiple clinical features.

HRQoL in long-term thyroid cancer survivors of was not inferior to that in healthy subjects. Preserved HRQoL, after long-term survivors of thyroid cancer presumably underwent standard treatment, and follow-up modalities should be considered in decision-making for cancer treatment, including both surgery and active surveillance.

CONFLICTS OF INTEREST

The statistical analysis was conducted by Medical Excellence Inc. No potential conflict of interest relevant to this article was reported.

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AUTHOR CONTRIBUTIONS

Conception or design: J.L., M.H.K. Acquisition, analysis, or interpretation of data: J.L., Y.J.L., D.J.L. Drafting the work or revising: J.L. Final approval of the manuscript: J.L., Y.J.L., D.J.L., J.M.L., S.A.C., M.H.K.

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REFERENCES

1. Miller KD, Siegel RL, Lin CC, Mariotto AB, Kramer JL, Rowland JH, et al. Cancer treatment and survivorship statistics, 2016. CA Cancer J Clin 2016;66:271-89.
2. Howlader N, Noone A, Krapcho M, Miller D, Brest A, Yu M, et al. SEER Cancer Statistics Review, 1975-2018 [Internet]. Bethesda: National Cancer Institute; 2021 [cited 2022 Aug 9]. Available from: https://seer.cancer.gov/csr/1975_2018/.
3. Jung KW, Won YJ, Kong HJ, Lee ES. Prediction of cancer incidence and mortality in Korea, 2019. Cancer Res Treat 2019;51:431-7.
4. Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, et al. 2015 American Thyroid Association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: the American Thyroid Association guidelines task force on thyroid nodules and differentiated thyroid cancer. Thyroid 2016;26:1-133.
5. Nickel B, Tan T, Cvejic E, Baade P, McLeod DS, Pandeya N, et al. Health-related quality of life after diagnosis and treatment of differentiated thyroid cancer and association with type of surgical treatment. JAMA Otolaryngol Head Neck Surg 2019;145:231-8.
6. Park J, Blackburn BE, Ganz PA, Rowe K, Snyder J, Wan Y, et al. Risk factors for cardiovascular disease among thyroid cancer survivors: findings from the Utah Cancer Survivors Study. J Clin Endocrinol Metab 2018;103:2468-77.
7. Blackburn BE, Ganz PA, Rowe K, Snyder J, Wan Y, Deshmukh V, et al. Aging-related disease risks among young thyroid cancer survivors. Cancer Epidemiol Biomarkers Prev 2017;26:1695-704.
8. Yin DT, He H, Yu K, Xie J, Lei M, Ma R, et al. The association between thyroid cancer and insulin resistance, metabolic syndrome and its components: a systematic review and meta-analysis. Int J Surg 2018;57:66-75.
9. Schultz PN, Stava C, Vassilopoulou-Sellin R. Health profiles and quality of life of 518 survivors of thyroid cancer. Head Neck 2003;25:349-56.
10. Crevenna R, Zettinig G, Keilani M, Posch M, Schmidinger M, Pirich C, et al. Quality of life in patients with non-metastatic differentiated thyroid cancer under thyroxine supplementation therapy. Support Care Cancer 2003;11:597-603.
11. Giusti M, Sibilla F, Cappi C, Dellepiane M, Tombesi F, Ceresola E, et al. A case-controlled study on the quality of life in a cohort of patients with history of differentiated thyroid carcinoma. J Endocrinol Invest 2005;28:599-608.
12. Tagay S, Herpertz S, Langkafel M, Erim Y, Bockisch A, Senf W, et al. Health-related quality of life, depression and anxiety in thyroid cancer patients. Qual Life Res 2006;15:695-703.
13. Tan LG, Nan L, Thumboo J, Sundram F, Tan LK. Health-related quality of life in thyroid cancer survivors. Laryngoscope 2007;117:507-10.
14. 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;93:200-3.
15. Maki Y, Horiuchi K, Okamoto T. Fatigue and quality of life among thyroid cancer survivors without persistent or recurrent disease. Endocr Connect 2022;11:e210506.
16. Pitoia F, Jerkovich F. Dynamic risk assessment in patients with differentiated thyroid cancer. Endocr Relat Cancer 2019;26:R553-66.
17. Yi KH. The revised 2016 Korean Thyroid Association guidelines for thyroid nodules and cancers: differences from the 2015 American Thyroid Association guidelines. Endocrinol Metab (Seoul) 2016;31:373-8.
18. Kim MH, Cho YS, Uhm WS, Kim S, Bae SC. Cross-cultural adaptation and validation of the Korean version of the EQ-5D in patients with rheumatic diseases. Qual Life Res 2005;14:1401-6.
19. Mozzi A, Meregaglia M, Lazzaro C, Tornatore V, Belfiglio M, Fattore G. A comparison of EuroQol 5-Dimension health-related utilities using Italian, UK, and US preference weights in a patient sample. Clinicoecon Outcomes Res 2016;8:267-74.
20. Lee YK, Nam HS, Chuang LH, Kim KY, Yang HK, Kwon IS, et al. South Korean time trade-off values for EQ-5D health states: modeling with observed values for 101 health states. Value Health 2009;12:1187-93.
21. Gao YJ, Li B, Wu XY, Cui J, Han JK. Thyroid tumor-initiating cells: increasing evidence and opportunities for anticancer therapy (review). Oncol Rep 2014;31:1035-42.
22. Megwalu UC, Moon PK. Thyroid cancer incidence and mortality trends in the United States: 2000-2018. Thyroid 2022;32:560-70.

23. Mitchell AL, Gandhi A, Scott-Coombes D, Perros P. Management of thyroid cancer: United Kingdom National Multidisciplinary Guidelines. J Laryngol Otol 2016;130(S2): S150-60.
24. Filetti S, Durante C, Hartl D, Leboulleux S, Locati LD, Newbold K, et al. Thyroid cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2019;30:1856-83.
25. Fugazzola L, Elisei R, Fuhrer D, Jarzab B, Leboulleux S, Newbold K, et al. 2019 European Thyroid Association guidelines for the treatment and follow-up of advanced radioiodine-refractory thyroid cancer. Eur Thyroid J 2019;8: 227-45.
26. Goswami S, Peipert BJ, Mongelli MN, Kurumety SK, Helenowski IB, Yount SE, et al. Clinical factors associated with worse quality-of-life scores in United States thyroid cancer survivors. Surgery 2019;166:69-74.
27. Kurumety SK, Helenowski IB, Goswami S, Peipert BJ, Yount SE, Sturgeon C. Post-thyroidectomy neck appearance and impact on quality of life in thyroid cancer survivors. Surgery 2019;165:1217-21.
28. Bongers PJ, Greenberg CA, Hsiao R, Vermeer M, Vriens MR, Lutke Holzik MF, et al. Differences in long-term quality of life between hemithyroidectomy and total thyroidectomy in patients treated for low-risk differentiated thyroid carcinoma. Surgery 2020;167:94-101.
29. Lee S, Kim HY, Lee CR, Park S, Son H, Kang SW, et al. A prospective comparison of patient body image after robotic thyroidectomy and conventional open thyroidectomy in patients with papillary thyroid carcinoma. Surgery 2014;156: 117-25.
30. Lee JA, Kim SY, Kim Y, Oh J, Kim HJ, Jo DY, et al. Comparison of health-related quality of life between cancer survivors treated in designated cancer centers and the general public in Korea. Jpn J Clin Oncol 2014;44:141-52.
31. Dingle IF, Mishoe AE, Nguyen SA, Overton LJ, Gillespie MB. Salivary morbidity and quality of life following radioactive iodine for well-differentiated thyroid cancer. Otolaryngol Head Neck Surg 2013;148:746-52.
32. Barbus E, Pestean C, Larg MI, Gabora K, Bonci EA, Badulescu C, et al. Psychological impact of 131I radioprotection measures on thyroid cancer patients. Clujul Med 2018;91: 441-7.
33. Shakir MK, Krook LS, Schraml FV, Hays JH, Clyde PW. Symptomatic hyponatremia in association with a low-iodine diet and levothyroxine withdrawal prior to I131 in patients with metastatic thyroid carcinoma. Thyroid 2008;18:787-92.
34. Schroeder PR, Haugen BR, Pacini F, Reiners C, Schlumberger M, Sherman SI, et al. A comparison of short-term changes in health-related quality of life in thyroid carcinoma patients undergoing diagnostic evaluation with recombinant human thyrotropin compared with thyroid hormone withdrawal. J Clin Endocrinol Metab 2006;91:878-84.
35. Borget I, Bonastre J, Catargi B, Deandreis D, Zerdoud S, Rusu D, et al. Quality of life and cost-effectiveness assessment of radioiodine ablation strategies in patients with thyroid cancer: results from the Randomized Phase III ESTIMABL Trial. J Clin Oncol 2015;33:2885-92.
36. Eustatia-Rutten CF, Corssmit EP, Pereira AM, Frolich M, Bax JJ, Romijn JA, et al. Quality of life in longterm exogenous subclinical hyperthyroidism and the effects of restoration of euthyroidism, a randomized controlled trial. Clin Endocrinol (Oxf) 2006;64:284-91.
37. Valle LA, Gorodeski Baskin RL, Porter K, Sipos JA, Khawaja R, Ringel MD, et al. In thyroidectomized patients with thyroid cancer, a serum thyrotropin of 30 μU/mL after thyroxine withdrawal is not always adequate for detecting an elevated stimulated serum thyroglobulin. Thyroid 2013;23: 185-93.
38. Massolt ET, van der Windt M, Korevaar TI, Kam BL, Burger JW, Franssen GJ, et al. Thyroid hormone and its metabolites in relation to quality of life in patients treated for differentiated thyroid cancer. Clin Endocrinol (Oxf) 2016;85:781-8.
39. Jung MS, Visovatti M. Post-treatment cognitive dysfunction in women treated with thyroidectomy for papillary thyroid carcinoma. Support Care Cancer 2017;25:915-23.
40. Lee JC, Song BS, Kang YM, Kim YR, Kang YE, Lee JH, et al. Effect of thyroid-stimulating hormone suppression on muscle function after total thyroidectomy in patients with thyroid cancer. Front Endocrinol (Lausanne) 2021;12:769074.
41. Pickard AS, Wilke CT, Lin HW, Lloyd A. Health utilities using the EQ-5D in studies of cancer. Pharmacoeconomics 2007;25:365-84.
42. Husson O, Haak HR, Mols F, Nieuwenhuijzen GA, Nieuwlaat WA, Reemst PH, et al. Development of a disease-specific health-related quality of life questionnaire (THYCA-QoL) for thyroid cancer survivors. Acta Oncol 2013;52:447-54.
43. Watt T, Hegedus L, Groenvold M, Bjorner JB, Rasmussen AK, Bonnema SJ, et al. Validity and reliability of the novel

thyroid-specific quality of life questionnaire, ThyPRO. Eur J Endocrinol 2010;162:161-7.
44. Bernardo DC, Li RJ, Jimeno C. Validity and reliability of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30: tagalog among adult filipinos with differentiated thyroid cancer. J ASEAN Fed Endocr Soc 2018;33:174-80.
45. Lee JI, Kim SH, Tan AH, Kim HK, Jang HW, Hur KY, et al. Decreased health-related quality of life in disease-free survivors of differentiated thyroid cancer in Korea. Health Qual Life Outcomes 2010;8:101.
46. Singer S, Lincke T, Gamper E, Bhaskaran K, Schreiber S, Hinz A, et al. Quality of life in patients with thyroid cancer compared with the general population. Thyroid 2012;22:117-24.
47. McIntyre C, Jacques T, Palazzo F, Farnell K, Tolley N. Quality of life in differentiated thyroid cancer. Int J Surg 2018;50:133-6.
48. Wang T, Jiang M, Ren Y, Liu Q, Zhao G, Cao C, et al. Health-related quality of life of community thyroid cancer survivors in Hangzhou, China. Thyroid 2018;28:1013-23.
49. Hirsch D, Ginat M, Levy S, Benbassat C, Weinstein R, Tsvetov G, et al. Illness perception in patients with differentiated epithelial cell thyroid cancer. Thyroid 2009;19:459-65.
50. Huang SM, Lee CH, Chien LY, Liu HE, Tai CJ. Postoperative quality of life among patients with thyroid cancer. J Adv Nurs 2004;47:492-9.