



Anxiety, depression and quality of life in patients undergoing total thyroidectomy: comparative analysis between differentiated thyroid cancer and benign nodular disease

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Abstract

Cancer is a condition that affects the psychological integrity of patients, due to the stigma that persists in relation to the disease. The aim of this study was to evaluate the presence of symptoms of anxiety, depression and the quality of life in patients undergoing total thyroidectomy for differentiated thyroid cancer and compare with patients undergoing total thyroidectomy for benign nodular disease. Cross-sectional study, conducted at the *Irmadade da Santa Casa de Misericórdia* in São Paulo, Brazil. A total of 64 patients submitted to total thyroidectomy were evaluated. Group A was composed of 29 patients with differentiated thyroid cancer and Group B was composed of 32 patients with benign nodular disease. Sociodemographic data were collected, Beck Anxiety Inventory (BAI) and Beck Depression Inventory (BDI) were used to identify symptoms of anxiety and depression. Quality of life was analyzed using Quality of Life Instrument (WHOQOL – BREF). The mean age was 49 ± 12 years, and 82.8% were female. Patients with differentiated thyroid cancer had higher levels of anxiety (BAI: 17.3 ± 11.4 vs. 10.3 ± 8.6) and depression (BDI: 12.6 ± 6.4 vs. 5.9 ± 7.2) compared to patients with benign nodular disease. The WHOQOL-BREF showed lower scores in the differentiated thyroid cancer group in relation to the benign nodular disease group for all domains evaluated: physical, psychological, social relationships, environment, self-assessment of quality of life, and general quality of life. Patients undergoing total thyroidectomy for differentiated thyroid cancer have more symptoms of anxiety and depression and a poorer quality of life when compared with patients undergoing total thyroidectomy due to benign nodular disease.

Keyword Cancer · Thyroidectomy · Thyroid · Anxiety · Depression · Quality of life

Introduction

Benign nodular disease and well-differentiated thyroid carcinoma are the most frequent conditions requiring thyroid surgery (Haugen et al., 2015). Thyroid cancer represents

1% of neoplasms in adults, and is the most common cancer of the endocrine system (Brito et al., 2011). Well-differentiated cancer and benign nodular disease of the thyroid gland share a similarity regarding treatment, which consists, in most cases, of total or partial removal of the thyroid gland. Beyond that, a malignant diagnosis may necessitate central or lateral neck dissection and complementary radioiodine therapy (Rosário et al., 2013).

After total thyroidectomy, the patient needs to take synthetic thyroid hormone to avoid hypothyroidism and between cancer patients, sometimes, as a suppression for Thyroid Stimulating Hormone (TSH) (Rosário et al., 2013). Generally, the dose adjustment process is easy, not causing significant harm. However, this process can become anxiogenic for the patient, once some habits changes are needed

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in the morning routine: after taking the medication, it is necessary to wait a certain period to ingest food or any other medication (Lira et al., 2014; Nascimento et al., 2015).

The prognosis for differentiated thyroid cancer (DTC), when compared to other types of malignant neoplasms, is usually better, but one cannot forget that, even once knowing the existence of well established, secure and efficient treatment, the stigma of cancer remains a synonym of pain, suffering and death. The diagnosis of any kind of cancer is still received followed by fear, anguish, anxiety and despair (Salci & Marcon, 2011). Patients diagnosed with DTC, even under follow-up with a specialist and with stable hormone levels, may report physical symptoms and intense psychological suffering due to the burden of malignancy diagnosis, with notable anguish and damage, especially in family and social life (Salci & Marcon, 2011; Bărbuș et al., 2017).

Cancer diagnosis provokes both physical and psychological distress to patients and their families (Vehling et al., 2022; Carlson et al., 2019; Zhu et al., 2017). The burden of facing a life-threatening disease and its treatment can interfere in social relationships and may lead to many negative consequences such as physical and mental exhaustion, mood disturbances, anxiety and depression (Vehling et al., 2022; Carlson et al., 2019; Zhu et al., 2017; Walker et al., 2014; Cordova, 1995; Derogatis et al., 1983; Kornblith, 1998; Moyer & Salovey, 1996; Stanton et al., 2001; Zabora et al., 2001; Hewitt et al., 2006; Adler et al., 2008; Reuben, 2004). The prevalence of any mental disorder is higher in cancer patients when compared to general population controls (odds ratio [OR], 1.28; 95% CI, 1.14 to 1.45) (Vehling et al., 2022). Such aspects lead to important impairment in quality of life and can also interfere in cancer treatment (Vehling et al., 2022; DiMatteo et al., 2011). Mental disorders such as anxiety and depression are routinely confounded as a normal reaction of facing cancer diagnosis, so on, the presence of psychological symptoms among cancer patients is usually underestimated, under-recognized and consequently under-treated (Fann et al., 2008; Forsythe et al., 2013).

Once cancer survival rates are increasing through time due to advances in treatment, recently, more effort is being driven to psychosocial aspects in oncology (Andersen et al., 2023). The presence of anxiety or depression leads to poorer quality of life in long term follow up among cancer patients after treatment (Vehling et al., 2022; Andersen et al., 2023). Even after surviving cancer, these patients can suffer from fear of recurrence or death for the rest of their lives and it may influence negatively on their adherence to the follow up, work capacity, work efficiency and social relationships.

Psychologically, it is possible to consider that the suffering of DTC patients may be more related to the stigma of the word "cancer" than to the biological behavior of the disease

(Goffman, 2006). This stigma leads patients to a distorted and biased perception of the diagnosis and, consequently, causes damage to their quality of life (Goffman, 2006). These aspects brings complexity to DTC patient care, and it is essential to health care professionals involved in the treatment to consider multiple factors along with patient evaluation, such as psychological, social, cultural, spiritual, and economic ones, as well as prejudices and taboos that may show throughout the course of the disease, even at the time of diagnosis (Lima et al., 2012).

There is a lack of robust studies, especially in national literature, regarding psychological aspects, including symptoms of anxiety and depression and the impact on the quality of life among patients who underwent thyroid surgery.

This study aims to compare the quality of life levels among patients undergoing total thyroidectomy for the treatment of malignant and benign thyroid disease using the WHO-QoL-Bref questionnaire and the Beck Inventories for anxiety and depression (Cunha, 2001; Fleck et al., 1999).

Methodology

A cross-sectional observational study included all patients with thyroid goiter and papillary thyroid carcinoma treated with a total thyroidectomy in a single reference hospital. The exclusion criteria were advanced malignant neoplasia (AJCC 8 ed. stage III and IV), malignant neoplasia with gross invasion of adjacent structures, cervical metastases requiring lateral neck dissection, Graves' disease, permanent vocal cord palsy, definitive hypoparathyroidism, tracheostomy, and other associated surgical procedures.

Sampling and recruitment

Convenience sampling was used to recruit the study patients. The surgical hospital registry was accessed to retrieve the list of all patients who met the inclusion criteria between January 2014 and December 2014. We contacted all the selected patients by phone, email, and postal letter to invite them to participate in the study.

Outcomes

The quality of life was evaluated with the WHOQOL-bref instrument, an abbreviated version of the World Health Organization Quality of Life Instrument 100 (WHOQOL-100). The WHOQOL-bref is a self-filled quality of life form containing 26 questions, one item for each 24 facets, and two general questions (Overall Quality of Life and General Health). The form provides a quality of life assessment divided into four domains: Physical Health; Psychological;

Social Relationships, and Environment. Each part is composed of facets that evaluate a specific aspect of the domain.

The outcomes of anxiety and depression were evaluated respectively with Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI); both instruments are validated in the Brazilian Portuguese language (Cunha, 2001). The Beck Inventory is a self-rating instrument that classifies symptoms of depression and anxiety into four categories: not present, mild, moderate, and severe.

Other variables

Clinical, demographic, and social data were collected as potential confounders and effect modifiers. Post-operative complications were also collected and considered in result analysis as confounders. Table 1 (Baseline Characteristics).

Data source

Between January 2015 and June 2015, all included patients were invited to an interview with the researchers, during which the quality of life, depression, and anxiety instruments were applied. Social and demographic data were also assessed in this interview. Clinical data and postoperative complications were collected from the medical record.

All eligible patients were invited to participate, received an explanation of the risks and aim of the study, and freely agreed to participate by signing the informed consent form.

This study was approved by the ethical committee of the institution.

Statistical analysis

The numeric and continuous variables were described with central tendency measures (mean, median, and interquartile interval). The categorical and ordinal variables were described with frequency and total count.

To evaluate the outcomes the patients were divided into two groups: Cancer and Benign. Univariate analyses were performed to evaluate imbalances between the groups in clinical, demographic, and social data. The normality distribution was tested with histogram, kurtosis, and skewness. The T-test was used for continuous variables and Pearson's chi-square test was used for ordinal/nominal variables.

The relationship between the predictors and the outcomes was evaluated with Treatment Effect regression. All the unbalanced variables, potential confounders, and effect modifiers were included in the regression model to adjust the results. The outcomes (WHOQOL-bref, BDI, BAI) were considered as count variables. The results of this analysis were reported as Average Treatment Effect (ATE).

Table 1 Baseline characteristics

Baseline Characteristics	Benign n=32	Cancer n=29	p
Age (mean; years)	52.5	44.65	0.0131
Postoperative time (mean; months)	8.25	9.275	0.4202
Gender			
Male	6 (19%)	3 (10%)	0.478
Female	26 (81%)	26 (90%)	
Marital Status			
Single	2 (6%)	6 (21%)	0.142
Married	21 (66%)	20 (69%)	
Widower	4 (13%)	0	
Divorced	2 (6%)	2 (7%)	
Common-law marriage	3 (9%)	1 (3%)	
Educational Stage			
Elementary School	19 (59%)	11 (38%)	0.139
High School	12 (38%)	14 (48%)	
Tertiary	1 (3%)	4 (14%)	
Religion			
Non-religious	2 (6%)	1 (3%)	0.138
Catholic	23 (72%)	19 (66%)	
Evangelical	4 (13%)	9 (31%)	
Spiritism	3 (9%)	0	
Children			
Yes	29 (91%)	25 (86%)	0.589
No	3 (9%)	4 (14%)	
Job Status			
Retired	8 (25%)	3 (10%)	0.427
Domestic job	10 (31%)	10 (35%)	
Regular employment	6 (19%)	7 (24%)	
Unemployed	1 (3%)	1 (3%)	
Self-employed	5 (16%)	8 (28%)	
Disability insurance	2 (6%)	0	
Psychological Support			
No	32 (100%)	27 (93%)	0.222
Yes	0	2 (7%)	
Speech Therapist Support			
No	32 (100%)	29 (100%)	
Yes	0	0	
Pathological Stage (AJCC 8ed)			
I		24 (82%)	
II		5 (17%)	
Pos Operative Complications			
Transient Hypocalcemia	0	1 (3.5%)	0.53
Seroma	1 (3.2%)	0	
Transient vocal cord palsy	0	1 (3.5%)	
Transient asymptomatic hypoparathyroidism (PTH=2.5 mg/dl)	1 (3.2%)	0	
Total	2 (6.3%)	2 (6.9%)	

Results

A total of 61 patients were included in the study, 32 patients in the benign group and 29 patients in the cancer group. All patients in the cancer group had a final pathological diagnosis of papillary thyroid carcinoma and were in the early pathological stage—AJCC 8th edition: 24 (82%) stage I and 5 (17%) stage II. Four patients (6.5%) had post-operative complications: one temporary hypocalcemia treated with oral calcium, one seroma, one transient vocal cord palsy, and one transient asymptomatic hypoparathyroidism (post-operative PTH=2.5 mg/dl). There were no statistical differences between both groups regarding complications. Table 1.

Baseline characteristics

The mean postoperative time was 8.2 months in the benign group and 9.3 months in the cancer group. The mean age was 52.5 years in the benign group and 44.6 years in the cancer group. In both groups, most of the patients were female (26/32, 81% benign; 26/29, 90% cancer), married (21/32, 66% benign; 20/29, 69% cancer), catholic (23/32, 72% benign; 19/29, 66% cancer), and had at least one child (29/32, 91% benign; 25/29, 86% cancer). Regarding the job status, the majority of patients labor in some way: domestic job (10/32, 31% benign; 10/29, 35% cancer), regular employment (6/31, 19% benign; 7/29, 24% cancer), and self-employed (5/31, 16% benign; 8/29, 28% cancer). Most patients had an educational level of elementary school (19/32, 59%) in the benign group and high school (14/29, 48%) in the cancer group. Only two patients received psychological support after the surgery, and none required speech therapist support.

The statistical analysis of baseline characteristics showed a significant difference only in the mean age of the groups (52.5 benign vs. 44.6 cancer, $p=0.01$); the remaining variables did not present differences between groups ($p>0.05$).

These results are shown in Table 1.

Beck inventory results

The average score of the BAI and BDI was significantly higher in the cancer group (BAI 11 benign vs. 17 cancer,

$p=0.04$; BDI 6 benign vs. 13 cancer, $p<0.001$). The cancer group had mild depression and moderate anxiety, while the benign group did not have depression symptoms and had mild anxiety. (Table 2, Fig. 1).

WHOQOL-bref results

The Cancer group had significantly lower scores in general questions and all domains evaluated by the WHOQOL-bref questionnaire. The general questions were: individuals' overall perception of quality of life (ATE [Cancer vs. Benign] -19%; $p=0.001$), and individuals' general perception of their health (ATE [Cancer vs. Benign] -16%; $p=0.008$). The evaluated domains were: Physical (ATE [Cancer vs. Benign] -20%; $p<0.001$), Psychological (ATE [Cancer vs. Benign] -19%; $p<0.001$), Social (ATE [Cancer vs. Benign] -21%; $p<0.001$), and Environment (ATE [Cancer vs. Benign] -17%; $p<0.001$). Figure 2 presents these results.

WHOQOL-bref facets

Physical domain The facets of “Energy and Fatigue” (ATE [Cancer vs. Benign] -33%; $p=0.000$), “Mobility” (ATE [Cancer vs. Benign] -17%; $p=0.009$), “Sleep and Rest” (ATE [Cancer vs. Benign] -17%; $p=0.015$), “Activities” (ATE [Cancer vs. Benign] -29%; $p<0.001$), and “Work Capacity” (ATE [Cancer vs. Benign] -29%; $p<0.001$) were statistically lower in the cancer group.

The facets of “Pain and Discomfort” (ATE [Cancer vs. Benign] -3%; $p=0.728$) and “Medication” (ATE [Cancer vs. Benign] -9%; $p=0.189$) did not significantly differ between groups.

Psychological domain The facet of “Thinking, learning, memory, and concentration” was the only one that did not significantly differ between groups. All the other facets in the Psychological domain were statistically lower in the Cancer group. These include “Positive feeling” (ATE [Cancer vs. Benign] -22%; $p<0.001$), “Spirituality / Religion / Personal beliefs” (ATE [Cancer vs. Benign] -14%; $p=0.004$), “Bodily image and appearance” (ATE [Cancer vs. Benign] -26%; $p<0.001$), “Self-esteem” (ATE [Cancer vs. Benign] -23%; $p=0.001$), and “Negative feelings” (ATE [Cancer vs. Benign] -18%; $p=0.016$).

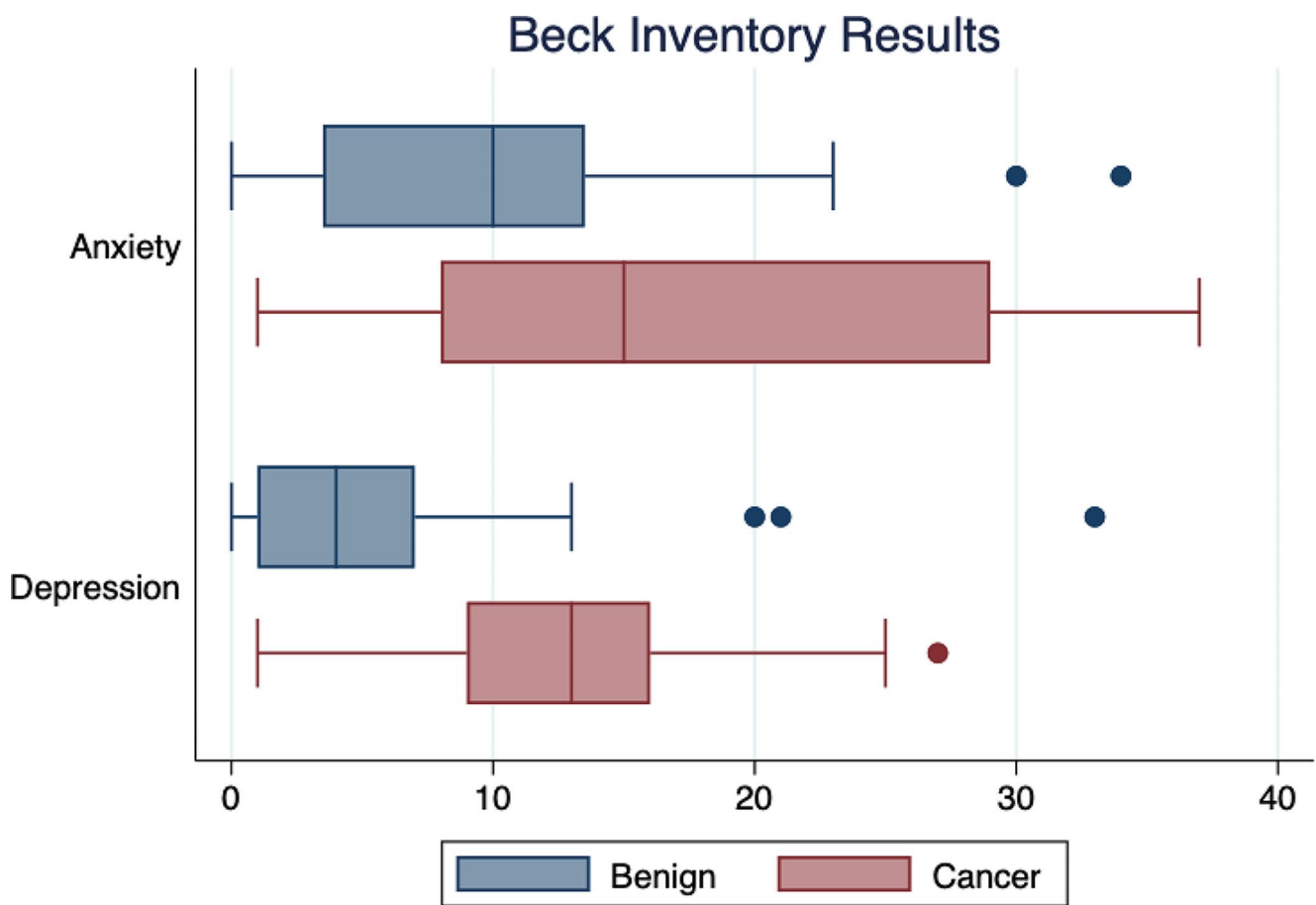
Social domain All the facets in the Social domain were statistically lower in the Cancer group: “Personal relationships” (ATE [Cancer vs. Benign] -27%; $p<0.001$), “Sexual activities” (ATE [Cancer vs. Benign] -17%; $p<0.001$),

Table 2 Beck inventory

Beck Inventory	Group (average score)		ATE* (Cancer vs Benign)	p
	Benign (N=32)	Cancer (N=29)		
Anxiety	11	17	6	0.04
Depression	6	13	7	0.00

Treatment effect with regression adjustment for age

*ATE: average treatment effect



Box plot of Beck Depression and Anxiety Inventory divided by groups.

Fig. 1 Box plot of Beck's Depression and Anxiety inventory divided by groups

and “Social support” (ATE [Cancer vs. Benign] -20%; $p < 0.001$).

Environment domain The Environment domain has eight facets; all had lower scores in the Cancer group. The facet “Opportunities for acquiring new information and skills,” and the facet “Transport” did not present statistical differences. All the other facets were statistically lower in the Cancer group: “Safety and security” (ATE [Cancer vs. Benign] -14%; $p = 0.009$); “Physical environment (pollution / noise / traffic / climate)” – (ATE [Cancer vs. Benign] -19%; $p = 0.001$); “Financial resources” (ATE [Cancer vs. Benign] -25%; $p < 0.001$); “Participation in and opportunities for recreation or leisure activities” (ATE [Cancer vs. Benign] -27%; $p < 0.001$); “Home environment” (ATE [Cancer vs. Benign] -18%; $p = 0.006$); and “Health and social care:

accessibility and quality” (ATE [Cancer vs. Benign] -18%; $p = 0.008$).

All the results were adjusted for age in multiple regression analysis. Table 3 resumes the WHOQOL-Bref results in both groups.

Discussion

In this cross-sectional sample, the quality of life was significantly impaired by the malignancy diagnosis in all domains and in global QoL and health status self-perception. Additionally, the anxiety and depression scores were also impaired in cancer group. This study only included patients with thyroid carcinoma in early stage, therefore the treatment (total thyroidectomy) was mainly the same for benign or cancer amplifying the theory that the cancer diagnosis has a significant impact on a patient's perception of life. This finding is in concordance with other literature noting improvements in QoL after surgery for benign disease but

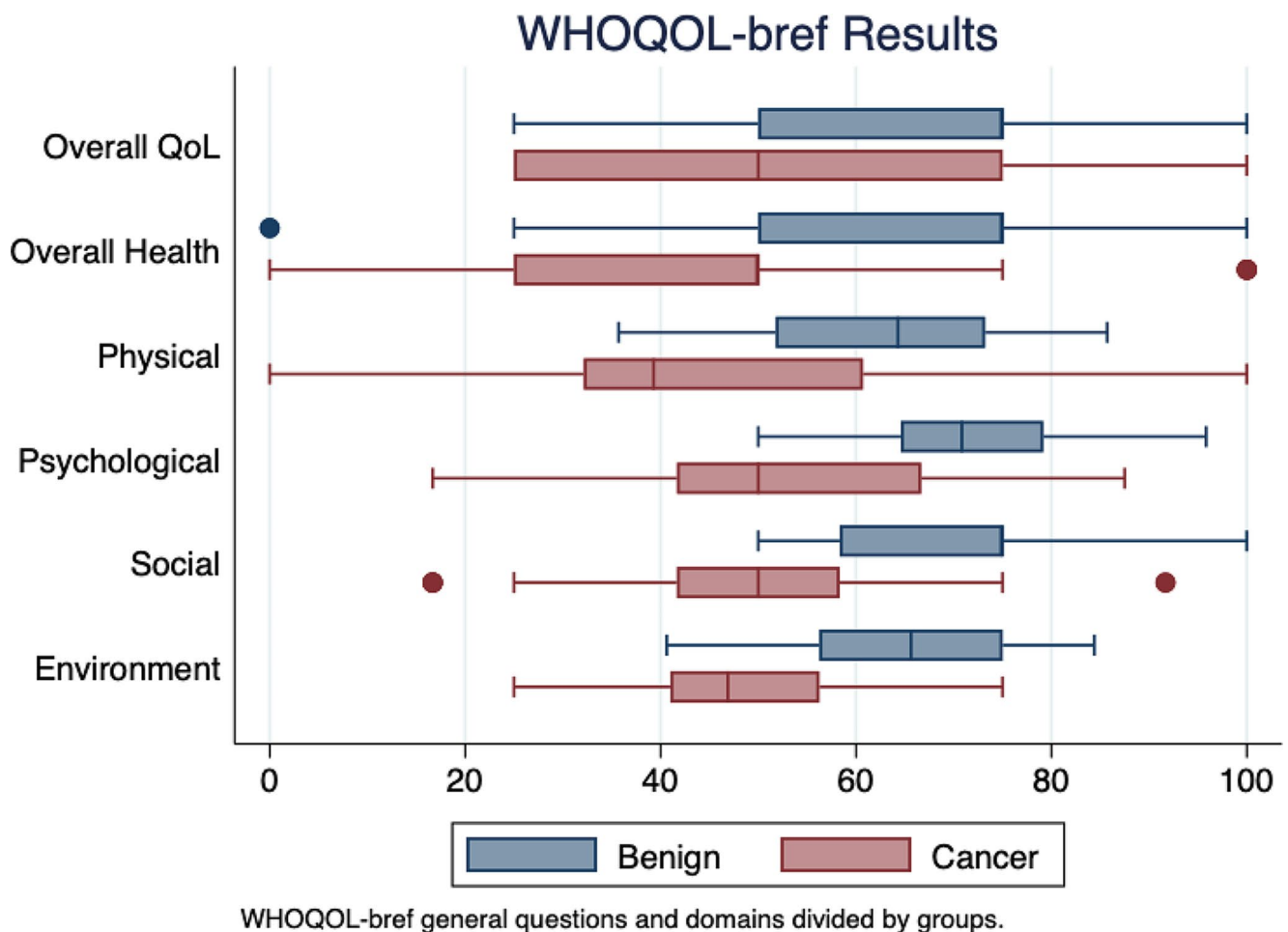


Fig. 2 WHOQoL general questions and domains divided by groups

decreases in QoL when surgery is performed for malignancy (Mirallié et al., 2020; Abdul-Sater et al., 2011).

Benign thyroid disease represents a heterogeneous population with varying levels of hormonal dysfunction. Symptoms, which may be due to a combination of anatomical or hormonal alterations, are non-specific and may not correlate with the underlying pathology. Given the increase in imaging completed for other purposes resulting in incidental findings of thyroid nodules, the vast majority of the current thyroid cancer diagnoses are made in the early stages of the disease. These malignancies are generally small nodules with no associated physical symptoms, and therefore baseline QoL scores in these patients may be higher than those who undergo thyroidectomy for bothersome goiters or enlarged symptomatic nodules. In patients with preoperative symptoms related to their thyroid disease, it is reasonable to expect a QoL improvement with treatment. An Australian study showed QoL improvement after surgical treatment of benign goiter in almost all domains after six months compared with preoperative status (Chew et al., 2020).

The same effect has not been seen in thyroidectomy performed for malignancy, as it has been well-published that thyroid cancer survivors have impaired QoL relative to the general population, and these deficits may persist for decades (Singer et al., 2012; Applewhite et al., 2016; Husson et al., 2013; Hoftijzer et al., 2008). Many authors have sought an explanation for these findings. Some authors pose that the differences may be due to hormonal disturbances, financial problems, and psychological disturbances (Kozíński et al., 2003). However, others have found these QoL differences were not associated with the rate of surgical complications or the need for hormone replacement in their study population (Abdul-Sater et al., 2011). Furthermore, a meta-analysis by (Landry et al., 2022) concluded that the decrease in QoL among thyroid cancer patients is present even in those undergoing active surveillance of their cancer rather than surgery (Landry et al., 2022). This suggests that the psychological impact of a cancer diagnosis has a greater impact than the treatment itself. This key principle is echoed by Jensen et al., who conducted interviews with patients, endocrinologists, and surgeons to examine their attitudes

Table 3 WHOQoL results

WHOQoL Results		Group (%) average score		ATE* (Cancer vs Benign)	p
		Benign (N = 32)	Cancer (N = 29)		
	Overall QoL	67	48	-19	0.001
	Overall health	58	42	-16	0.008
Facets	Physical Domain	61	42	-20	0.000
	Pain and discomfort	52	49	-3	0.728
	Medication: Dependence on medicinal substances and medical aids	50	41	-9	0.189
	Energy and fatigue	68	35	-33	0.000
	Mobility	69	52	-17	0.009
	Sleep and rest	59	42	-17	0.015
	Activities	65	37	-29	0.000
	Work capacity	65	36	-29	0.000
	Psychological Domain	71	52	-19	0.000
	Facets	Positive feelings	66	45	-22
Spirituality / Religion / Personal beliefs		82	68	-14	0.004
Thinking, learning, memory and concentration		66	56	-9	0.099
Bodily image and appearance		72	47	-26	0.000
Self-esteem		67	43	-23	0.001
Negative feelings		73	55	-18	0.016
Social Domain		71	49	-21	0.000
Facets		Personal relationships	73	46	-27
	Sexual activities	65	48	-17	0.000
	Social support	73	54	-20	0.000
	Environment Domain	64	47	-17	0.000
Facets	Safety and security: Freedom, physical safety and security	70	56	-14	0.009
	Physical environment (pollution / noise / traffic / climate)	67	49	-19	0.001
	Financial resources	62	37	-25	0.000
	Opportunities for acquiring new information and skills	65	59	-6	0.258
	Participation in and opportunities for recreation / leisure activities	62	35	-27	0.000
	Home environment	68	50	-18	0.006
	Health and social care: accessibility and quality	63	45	-18	0.008
Treatment effect with regression adjustment for age	Transport	56	45	-12	0.071

*ATE: average treatment effect

toward thyroid cancer diagnosis and management. This study found that hearing the word “cancer” evokes a strong negative reaction, along with fear and anxiety in some patients. Cultural norms and “default thinking” regarding a cancer diagnosis and its treatment may also influence patients’ self-perceptions about their health and quality of life (Jensen et al., 2020).

Another possible influence on post-operative QoL is the acceptance of one’s diagnosis. A study by Juzwizyn et al. using the same instrument WHO-QoL-BREF examined the variables of QoL, age, and acceptance of illness. They found significantly worse physical and psychological scores after surgery among these patients (Juzwizyn et al., 2020). These effects were especially pronounced in the elderly, with the worst quality of life and acceptance of illness scores. Although no conclusions were drawn correlating

poor acceptance of illness with worse QoL, other authors who have studied other chronic illnesses have found that acceptance of illness is an important prognostic factor in quality of life (Mazurek et al., 2022).

Our study has some limitations. Our sample included only patients who submitted to total thyroidectomy because it was performed in 2015, and at that moment the standard of care for thyroid carcinoma was total thyroidectomy in our center. QoL varies over time, many studies showed that as long the follow-up, less the impact of cancer diagnosis in QoL (Bärbuş et al., 2017; Hoftijzer et al., 2008; Landry et al., 2022). This was a cross-sectional study, so we were unable to evaluate these changes. However, the recruitment strategy, which includes the attendance of the researchers in all Head and Neck Surgery ambulatories in the study period, allowed us to include patients with a variety of baseline

characteristics and postoperative time, reducing the risk of selection bias.

Conclusion

In conclusion, this study showed that the malignancy diagnosis is associated with an impairment of all domains in QoL as well as self-perception of general QoL and health status. Likewise, it was associated with an increase in anxiety and depression scores.

Authors contributions Prof. Dr. Marianne Yumi Nakai—Idealization / Concept / Edition / Review.
Francisca Lúcia Passos Dantas- Idealization / Data collect / Concept / Drafting.
Dr. Lucas Ribeiro Tenório – Drafting / Edition / Review.
Prof. Dr. Antônio Jose Gonçalves—Drafting / Edition / Review.
Dr. Marcelo Benedito Menezes—Drafting / Edition / Review.
Antonio Augusto Tupinambá Bertelli – Drafting / Edition / Review.
Dr. Jonathon Russell – Edition / Review.
Dr. Samantha Wolfe—Edition / Review.

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Data availability All data were compiled using REDCap database where the study protocols were stored as well. In accordance to data protection policy these informations are not freely available, needing formal request to Santa Casa De São Paulo’s REDCap administrator to have access.

Declarations

Ethics approval This study has IRB approval from Santa Casa de São Paulo School of Medical Sciences (Number: 39628714.0.0000.5479 | 922.252) in accordance with the ethical standards of the committee on human experimentation of the Helsinki Declaration of 1975 (revised in 1983). All patients enrolled in this study gave written informed consent to participate in this study.

Consent to participate Informed consent was obtained from all individual participants included in the study.

Consent to publish This manuscript does not contain any individual person’s data in any form (including any individual details, images or videos).

Conflict of interest Prof. Dra. Marianne Nakai is a speaker for DMC Medical and Physiomed. Dr Antonio Bertelli is a speaker for Johnson&Johnson and Cook Medical. Dr Jonathon Russell is a consultant for Baxter Scientific. The other authors declare no conflict of interest.

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