QUALITY OF LIFE ASSESSMENT OF INDIVIDUALS WITH WELL-DIFFERENTIATED THYROID CARCINOMA USING WHOQOL-100*

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ABSTRACT: This study aimed to assess the quality of life of patients under clinical monitoring due to well-differentiated thyroid carcinoma using the WHOQOL-100 questionnaire. A quantitative, descriptive and cross-sectional study was undertaken between March 2015 and March 2017 in São Carlos, SP, Brazil, evaluating 280 individuals, being 70 suffering from thyroid carcinoma and 210 controls, divided in \leq 45 and >45 years. The results showed that the group with thyroid carcinoma \leq 45 years presented impairments in the physical domain (p=0.0032) and in the level of independence (p<0.0001), and improvements in the environment domain (0.0138). The group with thyroid carcinoma > 45 years presented improvements in the environment domain (0.0002) and in the global quality of life (p=0.00146) in relation to the controls. These findings, resulting from a comprehensive analysis of the quality of life of patients with differentiated thyroid carcinoma, can contribute to the understanding of the repercussions the disease and its treatment entail.

DESCRIPTORS: Quality of life; Thyroid neoplasms; Thyroidectomy; Surveys and Questionnaires; Health.

AVALIAÇÃO DA QUALIDADE DE VIDA DE INDIVÍDUOS COM CARCINOMA BEM DIFERENCIADO DE TIREOIDE PELO WHOQOL-100

RESUMO: Este estudo objetivou avaliar a qualidade de vida de pacientes em acompanhamento clínico por carcinoma bem diferenciado de tireoide, por meio do questionário WHOQOL-100. Trata-se de estudo quantitativo realizado entre março de 2015 e março de 2017 em São Carlos, SP, Brasil, descritivo e transversal, que avaliou 280 indivíduos, sendo 70 com carcinoma de tireoide e 210 controles, divididos em ≤45 e >45 anos. Os resultados mostraram que o grupo carcinoma de tireoide ≤ 45 anos apresentou prejuízo nos domínios físico (p=0,0032) e nível de independência (p<0,0001), e melhora no domínio meio ambiente (0,0138). O grupo com carcinoma de tireoide > 45 anos apresentou melhora no domínio meio ambiente (0,0002) e qualidade de vida global (p=0,00146) em relação aos controles. Esses achados, frutos de uma análise abrangente da qualidade de vida de pacientes com carcinoma diferenciado de tireoide, podem contribuir para o entendimento das repercussões da doença e seu tratamento. **DESCRITORES:** Qualidade de vida; Neoplasias da glândula tireoide; Tireoidectomia; Inquéritos e Questionários; Saúde.

EVALUACIÓN DE LA CALIDAD DE VIDA DE INDIVIDUOS CON CARCINOMA BIEN DIFERENCIADO DE TIROIDES MEDIANTE EL WHOQOL-100

RESUMEN: Este estudio objetivó evaluar la cualidad de vida de pacientes en seguimiento clínico por carcinoma bien diferenciado de tiroides, mediante el cuestionario WHOQOL-100. Se trata de estudio cuantitativo desarrollado entre marzo del 2015 y marzo del 2017 en São Carlos, SP, Brasil, descriptivo y trasversal, que evaluó 280 individuos, siendo 70 con carcinoma de tiroides y 210 controles, divididos en ≤45 y >45 años. Los resultados mostraron que el grupo carcinoma de tiroides ≤ 45 años presentó perjuicio en los dominios físico (p=0,0032) y nivel de independencia (p<0,0001), y mejora en el dominio medio ambiente (0,0138). El grupo con carcinoma de tiroides > 45 años presentó mejora en el dominio medio ambiente (0,0002) y calidad de vida global (p=0,00146) con relación a los controles. Eses hallazgos, frutos de un análisis amplio de la calidad de vida de pacientes con carcinoma diferenciado de tiroides, pueden contribuir a la comprensión de las repercusiones de la enfermedad y su tratamiento. **DESCRIPTORES:** Calidad de vida; Neoplasias de la tiroides; Tiroidectomía; Encuestas y Cuestionarios; Salud.

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INTRODUCTION

In 1995, the World Health Organization (WHO) defined the term quality of life (QoL) encompassing all existing concepts and what should be contained in the construct. The globally accepted concept defines QoL as "the individual's perception of cultural, social, political, and economic influences in the context of his life, which promotes the attainment of his goals, projects and expectations, and gives him opportunities for choices" (1:28). The formulation of the term considers QoL as a broad concept, incorporated into physical health, psychological condition, independence level, social relationships, personal beliefs and significant aspects of the environment (1).

Thyroid carcinoma (TC) stands out among the pathologies that affect QoL⁽²⁾. Annually, about 620 thousand patients⁽³⁾ are diagnosed with head and neck carcinoma, and TC is the most common neoplasm in this anatomical region. This represents 1% of all malignant tumors in the age group of 30 to 74 years and was the carcinoma that has grown most in terms of incidence in recent years⁽⁴⁾.

Of the more than 500 thousand new cases of malignancy estimated for 2016 in Brazil by the National Cancer Institute (INCA)⁽⁵⁾, 1,090 will be new cases of TC in males and 5,870 in females. Well-differentiated thyroid carcinoma (DTC), represented by papillary and follicular carcinomas, accounts for 90% of all TCs and has a favorable prognosis of 95% cure, with a lifetime risk of relapse of up to 25%⁽⁶⁾.

Thyroid malignancies and their treatment can lead to significant alterations in vital functions related to feeding, communication and social interaction of the affected individuals, and can generate important psychological repercussions, both for patients and their relatives, leading to some degree of dysfunction in their daily life^(2,7).

Treatment for DTC includes surgery, radiotherapy or a combination of these modalities⁽⁸⁾. In most cases of DCT, the surgical procedure indicated is the ablative thyroid surgery (or thyroidectomy) with removal of local lymph node metastases, followed by radioactive iodine therapy (RIT)⁽⁹⁾. These interventions often have undesirable physical and psychological consequences for individuals^(8,10), which are not always controllable⁽⁸⁾ and may have a negative impact on their QoL⁽²⁾. It is suggested, however, that the QoL of these patients tends to return to normal over the years⁽¹¹⁻¹²⁾.

As DTC is one of the most common carcinomas in Brazil⁽¹³⁾, evaluating the QOL of patients with treated DTC may help to better understand the actual impact of this pathology and how its treatment interferes in these individuals' lives⁽⁷⁾. Thus, this study aimed to evaluate the QoL of patients with treated DTC, in regular oncologic follow-up, through the WHOQOL-100 questionnaire.

METHOD

A quantitative, descriptive and cross-sectional study was carried out with two groups of patients: 1) patients treated for thyroid papillary carcinoma (CaT), that is, who underwent total thyroidectomy (TT) and radiotherapy more than one year earlier; without signs of active disease at the time of the research, in regular clinical follow-up; 2) control group (C), matched by age and sex with the CaT group, with three control individuals for each case. These groups were subdivided into two subgroups: less than or equal to 45 years or older than 45 years.

Group C included healthy patients, male and female, older than 18 years; Group CaT group included patients with well-differentiated thyroid carcinoma, treated at least one year earlier, who underwent TT, in regular follow-up at the oncology surgery outpatient clinic and on regular use of thyroid medication. Patients treated less than one year earlier and who did not undergo regular hormone replacement were excluded from the study.

The number of participants was delimited based on the access to patients and their consent to participate in the study, as well as the regularity of their clinical follow-up. Individuals answered two self-completed questionnaires without interference from the researcher. The evaluation was structured in two parts: the application of a questionnaire for the evaluation of clinical and sociodemographic data, including age, sex, education, marital status and presence of some associated pathology; application

of the World Health Organization Quality of Life Questionnaire (WHOQOL-100) - Portuguese version.

The WHOQOL-100 is a QoL measuring instrument developed in 1998 by the World Health Organization (WHO)⁽¹⁾, consisting of 100 questions divided into six domains and 24 facets: physical (pain, discomfort, energy and fatigue, sleep and rest); psychological (positive feelings, thinking, learning, memory, concentration, self-esteem, body image and physical appearance and negative feelings); level of independence (mobility, daily activities, dependence on medication or treatments, and work capacity); social relationships (personal relationships, social support and sexual activity); environment (physical safety, family environment, financial resources, health care, social service, recreation / leisure, physical environment and transportation); and spirituality (spiritual aspects, religion, personal beliefs).

The WHOQOL-100 results were expressed by the scores attributed to each facet and domain. In the descriptive analysis, the categorical data were summarized in absolute and relative frequencies and the numerical data in average, standard deviation (SD) and standard error of the mean (SEM). In the figures, the data were presented as mean ± standard error. The differences between the averages of the quantitative variables (different domains of the QoL questionnaires) were evaluated using the Kruskal-Wallis test, with Dunn post-test, using the program GraphPad prism 5°.

Multiple correlation analyses were also carried out to identify the strongest correlation between the domains and the global QOL. The value of the regression parameter indicating significant correlation was defined as> 0.3. In all tests, significance was set at 5%.

The research received approval from the Ethics and Research Committee (CEP) with Human Beings of the Federal University of São Carlos (opinion 1207421) and by the Municipal Health Department of São Carlos (opinion DRCA 394/2015).

RESULTS

The study included 280 participants, aged 24-86 years. Of these, 240 (85.7%) were women older than 45 years (n = 160, 57.1%). The mean age in group C was 47.32 ± 0.84 years and in CaT 48.41 ± 1.51 years. In addition, 87 patients (41.5%) from group C and 40 (56.8%) from CaT did not report any associated pathology. All subjects in the CaT group underwent TT treatment followed by radiotherapy, 41 participants (58.6%) supplemented the TT with cervical voiding. The mean interval between treatment and participation in the study was 5.2 ± 0.4 years. Regarding the histological type of the tumor, papillary carcinoma predominated (85.7%).

Table 1 shows the mean \pm standard deviation (SD), standard error of the mean (SEM) and p-value of the WHOQOL-100 domains in the different groups studied. The Spirituality domain presented the highest mean in the four subgroups studied, followed by the Independence domain in group C \leq 45 years (76.02), global QoL in the CaT group> 45 years (72.66) and in the CaT group> 45 years (72.18). Significantly higher domains were the physical (p = 0.003) in group C \leq 45 years in relation to CaT; independence in group C \leq 45 years (p <0.0001) in relation to CaT; environment in groups CaT \leq 45 years (p = 0.01) and CaT> 45 years (p = 0.0002) in relation to groups C of the same age ranges; QoL in the CaT group> 45 years (p = 0.02) in relation to group C.

Table 1 – Means, standard deviations and standard errors of the mean for the domain and general QoL scores and p-values. São Carlos, SP, Brazil, 2017 (continues)

Domain	Age range	Group	Mean	SD	SEM	р
Physical	≤ 45 years	С	62.06	19.05	2	0.003*
		CaT	50.46	18.44	3.36	
	>45 years	С	59.10	16.89	1.54	0.56
		CaT	56.56	15.23	2.40	

Psychological	≤ 45 years	С	64.15	14	1.47	0.56
, 0	· -	CaT	63.31	15.16	2.76	_
	>45 years	С	65.80	12.31	1.12	0.53
	-	CaT	67.03	13.63	2.15	_
Independence	≤ 45 years	С	76.02	16.63	1.75	<0.0001*
		CaT	61.28	14.62	2.69	
	>45 years	С	68.22	16.86	1.53	0.29
		CaT	64.62	15.48	2.44	
Relationships	≤ 45 years	С	67.50	13.50	1.42	0.22
		CaT	71.62	15.47	2.82	
	>45 years	С	70.45	13.12	1.19	0.45
		CaT	72.18	14.66	2.31	
Environment	≤ 45 years	С	56.35	9.354	0.98	0.01*
		CaT	63.66	11.74	2.14	
	>45 years	С	59.07	10.31	0.94	0.0002*
		CaT	65.20	9.716	1.53	
Spirituality	≤ 45 years	С	83.54	18.70	1.97	0.88
		CaT	84.44	15.60	2.84	
	>45 years	С	82.86	19.10	1.74	0.69
		CaT	83.44	15.54	2.45	
Global QoL	≤ 45 years	С	66.11	15.84	1.67	0.90
		CaT	66.25	17.23	2.72	
	>45 years	С	66.88	14.12	1.28	0.02*
		CaT	72.66	14.41	2.27	

Source: Research data, 2017. * p-value with statistical significance.

In Table 2, the multiple correlation coefficients and p-values resulting from the domain analysis in relation to the global QoL are displayed, in the four subgroups of the study. The domains with the highest significant correlation coefficient with the global QoL were: in groups $C \le$ and >45 years, the psychological (r=0.01; p=0.02), social relationships (r=0.01; p=0.028) and environment domains (r=0.07; p=0.01); in group CaT >45 years the psychological domain (r=0.42; p=0.01). The group CaT >45 years did not present domains that were significantly correlated with the global QoL.

Table 2 – Multiple correlation coefficients (r) and respective p-value of the domains in relation to the global QoL of the groups studied. São Carlos, SP, Brazil, 2017

Domain		Group C				Group CaT			
	≤ 45 y	≤ 45 years		> 45 years		≤ 45 years		> 45 years	
	r	р	r	р	r	р	r	р	
Physical	0.01	0.93	0.09	0.29	0.29	0.14	0.21	0.19	
Psychological	0.39	0.01*	0.28	0.02*	0.10	0.74	0.42	0.01*	
Independence	0.03	0.71	0.07	0.39	-0.13	0.57	0.02	0.89	
Relationships	0.35	0.01*	0.20	0.03*	0.17	0.48	0.07	0.61	
Environment	0.24	0.07*	0.31	0.01*	0.41	0.22	0.26	0.15	
Spirituality	0.0006	0.99	0.05	0.29	0.19	0.20	0.09	0.30	

Source: Research data, 2017. * p-value with statistical significance.

Figure 1 shows the variations in the WHOQOL-100 scores between the C and CaT groups in each statistically significant domain. In Figure 2, the domains are displayed in which C>CaT: (a) physical in the individuals \leq 45 years (p=0.0032) and (b) independence in individuals \leq 45 years (p<0.0001).

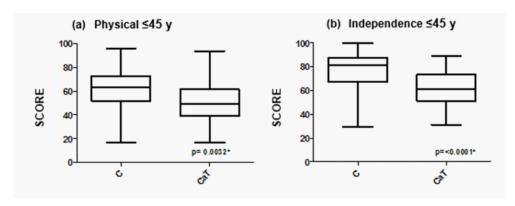


Figure 1 – Comparative boxplot of WHOQOL 100 scores between domains in which C>CaT: (a) physical domain \leq 45 years C>CaT (p=0.0032*) (b) independence domain \leq 45 years C>CaT (p<0.0001*). *statistically significant difference between groups C and CaT. São Carlos, SP, Brazil, 2017

In Figure 2, the domains are shown in which CaT>C: (a) environment in individuals \leq 45 years (p= 0.0138), (b) environment (p=0.0002) and (c) global QoL (p= 0.0146) in individuals >45 years.

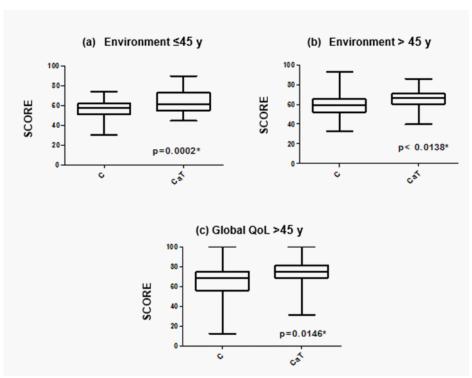


Figure 2 – Comparative boxplot of WHOQOL 100 scores between domains in which CaT>C: (a) environment domain \leq 45 years CaT>C (p=0.0002*) (b) environment domain >45 years CaT>C (p<0.0138*) (c) global QoL domain >45 years CaT > C (p=0.0146*). *statistically significant difference between groups C and CaT (p=0.0146). São Carlos, SP, Brazil, 2017

DISCUSSION

In this study, the QoL of patients with treated DTC could be evaluated. The results indicate that the overall QoL of the CaT group> 45 years was higher than that of the C group, and that the environmental domain score was higher in the CaT patients in both age groups. In the physical and independence domains \leq 45 years, the CaT group obtained lower scores.

In the physical domain, the results showed that, although the general QoL of patients with DTC can be equal to or even better than that of the general population, the physical impact of the disease is still considered relevant and is reflected in the decrease in the domain scores⁽¹²⁾. The symptoms resulting from the disease and its treatment affect patients' daily life and do not appear in isolation, as they are usually accompanied by physical signs resulting from the treatment⁽¹⁴⁻¹⁵⁾. Manifestations such as fatigue, insomnia, pain and depression occur frequently⁽¹⁶⁻¹⁷⁾, and living with this health condition is challenging. Some years after the surgery, it appears that the wellbeing of these individuals tends to re-establish. Patients with DTC treated longer (≥ 5 years since diagnosis) feel less tired when compared to those treated less than 5 years earlier⁽¹²⁾. The effects resulting from the treatment can be minimized through interventions such as a specific exercise program / physical activity practice and optimization of the treatment to reduce fatigue⁽¹⁷⁾, which is a frequent complaint of these individuals.

The psychological domain was not affected in this study. A survey of 16 adolescents with DST corroborates our findings, pointing out that the respondents had QoL and anxiety levels similar to healthy individuals⁽¹⁹⁾. Another result indicates a correlation between this domain and the global QoL in the CaT group> 45 years, which suggests that the QoL of these patients suffers important influence from the psychological domain. Therefore, the psychological monitoring of these individuals is necessary throughout the carcinoma treatment and follow-up. The support of the spouse, family and friends helps in the process of coping and in the emotional stability of these patients⁽²⁰⁾.

The domain level of independence obtained lower scores in the CaT group \leq 45 years. Patients treated with DTC need lifelong care. This, together with the need for long-term follow-up and the possibility of future recurrence of the disease, is a source of concern for survivors, especially younger ones⁽²¹⁾. Thyroidectomy surgery, however, does not entail consequences that prevent subjects from performing their work inside and outside the home, or their activities of daily living⁽²²⁾.

Despite reports of changes in the type of work⁽¹⁹⁾ due to the pathology, being employed seems to have a positive influence on the functioning of this social dimension⁽²³⁾. One of the facets evaluated in this area is mobility. According to the background literature and the results of this study, it can be concluded that the decrease in the scores for this facet is related to the fatigue and decreased energy referred by these patients, which impair their locomotion and interfere in their daily life⁽²⁴⁾.

Another impact in the domain level of independence is related to the financial segment. The need for supplementation with thyroid hormones and continuous adjustments of the medication cause psychological and financial costs for individuals. From the financial point of view, this type of carcinoma is one of the most costly and the younger patients, financially less stable, may present concerns or stress regarding the purchase of these drugs⁽¹⁵⁾.

Authors⁽²⁵⁾ also evidenced a negative association between the use of hormone replacement drugs and QoL. Other studies that also evaluated the repercussions of drug treatment showed that patients had similar or slightly decreased QoL compared to the general population⁽¹⁴⁾. Therefore, the treatment planning agreed upon with the patient and family is critical.

No impairments were found in the social relationships domain. Family and social support was reported by the patients as very positive and they reported the strengthening of family ties after the diagnosis of the disease⁽¹⁸⁾. In addition to health care, family and friends provide the emotional support needed throughout the treatment of the disease. Churches and the community can also give material and spiritual support. Being supported makes a difference in the lives of these patients and, faced with this challenging situation, this can result in greater emotional balance⁽²⁶⁾.

Patients in group C had a significantly lower score in the environmental domain than in the CaT group. The difference in scores observed suggests that individuals in the CaT group, perhaps because they have greater social and family support, besides benefits guaranteed by Brazilian legislation, have fewer difficulties in the aspects concerning this domain⁽²⁷⁾.

This study highlights spirituality as a factor that positively influences the individuals' wellbeing. This domain obtained a higher average in all the groups studied and reveals spirituality as a relevant factor in the trajectory of the individuals' life, besides being clinically acknowledged as important in the adaptation and survival after the carcinoma⁽²²⁾.

Spirituality and religiosity are highlighted as a fundamental coping mechanism after the discovery of a malignant disease⁽²²⁻²⁸⁾, with potential to facilitate the psychological adaptation to the tumor and to reduce depressive symptoms⁽²⁸⁾. Research shows that⁽²⁰⁾ religiosity and spirituality are effective strategies to face the suffering the cancer causes, as well as a source of hope and re-signification of the meaning of life.

The CaT group of patients ≤45 years old did not present any domain associated in isolation with their QoL, but the sum of the effects of each domain was responsible for 97.5% of the variability in their global QoL. This means that comprehensive actions are necessary to increase the QoL of these individuals and that surveillance of all domains should be undertaken to ensure the maintenance of their QoL. On the other hand, in the CaT group> 45 years, global QoL showed a greater correlation with the psychological domain, indicating that these patients particularly need support in this regard.

Overall QoL had a higher score in the CaT group> 45 years compared to the C group, with no differences between the CaT groups \leq 45 years and their controls. Several factors may be related to this finding, such as: being involved in a job activity⁽²⁹⁾; positive behavioral and positive worldview changes after the cancer experience⁽¹⁸⁾, with adherence to healthy behaviors such as physical activity practice⁽¹⁷⁾; time elapsed after diagnosis and treatment of DTC⁽¹⁴⁾; family and social support⁽²⁶⁾; measures of financial support guaranteed by Brazilian legislation.

The literature points to the diversity of results related to QoL and DTC. An integrative review⁽¹⁴⁾, which aimed to analyze the association between DTC and QoL, identified contradictory results. Some studies have shown that QoL is decreased in DTC survivors compared to the healthy population or other reference groups, while others found an opposite result, which was the case in the present study^(12,30).

Thus, further research is needed to assess the current QoL of DTC in the face of advances in its diagnosis and treatment and to more accurately determine the factors not related to health that influence it, as patients with DTC perceive their disease in a much more subjective and emotional than objective manner.

The limitation of this study is the reduced number of male participants, as a result of the difference in the prevalence of the disease in terms of gender. In addition, there is a lack of recent research using the WHOQOL-100 to support some items in the discussion and to determine the non-health factors that influence the QoL more precisely.

FINAL CONSIDERATIONS

Elements that emerged from the data analysis of this study permitted reinforcing that some practices may have a positive effect on the QoL of individuals with DTC, such as: (1) adoption of measures that facilitate the patients' daily life and interventions to stimulate the practice of physical activity; (2) psychological counseling throughout the treatment, for patients and their families; (3) appropriate guidelines on DTC and its treatment in order to reduce the anxiety and tension caused by the uncertainties that the advent of carcinoma can generate; (4) individualized and agreed treatment planning, including the family of these patients; and (5) provision of appropriate information about the rights of the patient with DTC, in order to assure individuals of all the benefits guaranteed by Brazilian legislation.

Recent studies using the WHOQOL-100 instrument, which is more complete and more comprehensive than the health-related questionnaires, have not been found in the literature to study the QoL of patients with treated DTC. The present results, therefore, add new elements to the existing bibliography in order to support the discussions on this very complex theme.

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