

Quality of life profile three months or more after the end of adjuvant radiotherapy used for the treatment of head and neck cancer in a High Complexity Oncology Care Center

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Abstract

The treatment of head and neck cancer (HNC) is multimodal and can generate different physical and psychological impairments. The aim of this study was to assess the quality of life profile of patients with HNC, in search of possible therapeutic targets that can be improved. This is a descriptive, cross-sectional, observational study, developed at a High Complexity Care Center in Oncology. Data were collected through anamnesis and the University of Washington quality of life questionnaire (UW-QOL). The sample consisted of 68 patients with head and neck cancer who underwent adjuvant radiotherapy for at least 90 days. There was a predominance of males (89%) and an involvement of the oropharynx (69%). In addition to radiation therapy, 53% of individuals also underwent surgery and 65% chemotherapy. Stomatognathic functions were the most affected, followed by negative implications related to activities of daily living and psychological aspects. According to the nature of the domains found in the UW-QOL Questionnaire, the low scores observed in the questions related to the activities of daily living and in the components of the psychological status assessment, it is pertinent to assume that the late complications imposed by both the pathophysiology of the HNC as well as the antineoplastic treatment should be approached by a multidisciplinary team aligned with the synergistic objective of rehabilitating stomatognathic functions, nutrition, and physical capacity. Although our data do not suggest emotional impairments, additional support from a psychologist could be considered in order to strengthen and motivate engagement in the rehabilitation of the complex clinical condition intrinsic to HNC.

Keywords: Head and Neck Neoplasms. Health-Related Quality of Life. Disease Impact Profile. Adverse effects. Drug-Related Side Effects and Adverse Reactions. Rehabilitation. Radiation therapy.

INTRODUCTION

Currently, cancer represents the disease that is responsible for the largest number of deaths in the world, with an estimated incidence of 600,000 new cases for the 2018-2019 biennium¹. One of the most prevalent types is head and neck cancer (HNC), a fact that has been arousing the interest of authorities, especially in campaigns that

promote prevention and self-care².

The treatment of HNC is most often multimodal and may involve two or more of the following categories simultaneously: surgery, chemotherapy, and radiation therapy³. Radiation therapy aims to destroy tumor cells through ionizing radiation, but despite being a more localized treatment

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in the tumor region, it ends up affecting adjacent healthy cells, thus causing adverse effects⁴⁻⁵.

Patients undergoing these treatments, especially surgery and radiation therapy, may have physical and psychological impairments⁶. These impairments affect swallowing, speech, mouth opening (trismus), face and neck movements, as well as the loss of strength and shoulder range of motion⁷⁻⁹. From a psychological point of view, changes in body image, frequent in patients who undergo extensive surgeries, are negatively associated with a decrease in quality of life, largely due to aesthetic changes, but also due to the lymphedema that appears as one of the main late effects together with fibrosis¹⁰. Late treatment effects are often progressive and directly influence the long-term quality of life of these patients¹¹.

In addition to antineoplastic interventions, multidisciplinary teams, which provide therapeutic support in the long-term management of HNC survivors, should consider the negative impact that the observed impairments on quality of life (QL) have on patient adherence to the follow-up treatments. In the meta-analysis published by Michaelsen *et al.*¹², 1,366 patients enrolled in 25 studies carried out in 12 countries, revealed that the main damages are markedly centered on xerostomia, dysphagia, and mastication¹²⁻¹⁴.

In recent decades, the attempt to improve the prognosis of these patients resulted in the development of guidelines in which the joint effort of multidisciplinary teams of collaborators describe different strategies for managing the long-term side effects induced by the treatment of HNC¹⁵. Among these guidelines are 1) ways of supporting patients and fear of their partners in relation to cancer, 2) reinforcement of the need to provide coordinated care among all physicians involved, 3) assessment of patients' needs from multidisciplinary teams, and 4) the

institution of measures to guarantee access to high-quality treatments. The transition to the return to primary care was also identified as fundamental to improve the distribution of survival care¹⁶⁻¹⁸. In general, the subsequent steps of continuous treatment need specialized attention.

The need for antidepressant treatment is frequent in these patients¹⁹ and, in this sense, different approaches to psychological treatments^{19,20} have shown positive effects on QoL, as well as emotional and social function. The patient's motivation is fundamental for the maintenance and adherence to the treatment in several aspects. Among them, functional capacity, regardless of the form of assessment²¹ (Karnofsky Performance Status (KPS), Eastern Cooperative Oncology Group (ECOG), Performance Status and/or Palliative Performance Scale (PPS)) is an important parameter for predicting oncological patient survival. Therefore, the rehabilitation of functional capacity through interventions based on physical exercise has demonstrated significant benefits in different criteria that make up the quality of life questionnaires for cancer survivors²².

Mishra *et al.*¹⁸ reviewed 40 clinical trials where participants with different cancer diagnoses (breast, colorectal, head and neck, lymphoma, and others) were randomized into an exercise (n = 1927) or comparison group (n = 1764), and observed that exercise has a positive impact on overall quality of life (0.48; 95%CI 0.16 to 0.81), body image/self-esteem when assessed by the Rosenberg Self-esteem scale (4.50; 95%CI 3.40 to 5.60), emotional well-being (0.33; 95%CI 0.05 to 0.61), sexuality (0.40; 95%CI 0.11 to 0.68), sleep disturbance (-0.46; 95%CI -0.72 to -0.20), and social function (0.45; 95% CI 0.02 to 0.87). There was also a decrease in anxiety (-0.26; 95% CI -0.07 to -0.44), fatigue (-0.82; 95% CI -1.50 to -0.14), and pain (-0.29; 95% CI -0.55 to -0.04). Using linear mixed effects analysis models, Buffart *et al.*¹⁹ observed,

in a sample of 4,519 patients, significant improvements in quality of life ($\beta = 0.15$, 95%CI = 0.10; 0.20) and physical function ($\beta = 0.18$, 95%CI = 0.13; 0.23) regardless of demographic and clinical characteristics, or even the shape of the muscular overload. An important fact is that the effect of physical exercise is greater when performed in a supervised manner^{18,19} or when the energy expenditure prescribed in unsupervised exercise programs is greater²³.

Assessing the QoL in patients with HNC is important not only to describe the issues

inherent to this population, but it is also an objective way to point out the most present needs in this population, thus, helping to develop therapeutic proposals consistent with the real needs of this population, in order to reduce sequelae, and provide preventive measures²⁴.

Therefore, this study aimed to assess the quality of life of these patients through a questionnaire specifically designed for this population, as a way to identify possible therapeutic targets to be treated in a rehabilitation program.

METHODS

In this cross-sectional, descriptive, and observational study, carried out in a High Complexity Care Center in Oncology (Santa Rita Hospital of the Irmandade Santa Casa de Misericórdia complex in Porto Alegre), 68 patients in the late phase (90 days or more) concluding adjuvant radiotherapy used for the treatment of HNC were included. The study was approved by the Research Ethics Committee of the Institution (CAAE: 51070115.4.3001.5345) and all patients received and signed an informed consent form prepared, evaluated, and approved as determined by Resolution 466/12. All volunteers were evaluated through the anamnesis where the clinical data relevant to the study were cataloged and described later in table 1. For the assessment of quality of life, the University of Washington – Quality of Life (UW-QOL) questionnaire was used, which was validated for the Brazilian population by Vartanian *et al.*²⁵.

The questionnaire used is composed of 12 domains, in which there are between 3 and 5 response options with scores ranging from zero to one hundred (0 - 100). This instrument has 3 questions about self-

perceived quality of life and a descriptive question for additional considerations. To present the various aspects of the UW-QOL, the questions were grouped in relation to stomatognathic functions (saliva, taste, swallowing, chewing, and speaking), activities of daily living (activities in general, recreational activities, shoulder movement, and interference from pain in routine physical activities of the day), and perceptions of damage to psychological conditions (mood, appearance, and anxiety). Whenever possible, the filling out of the questionnaire was carried out individually and without assistance. If necessary, a member of the research team read aloud the questions and the corresponding answer options.

The normality of data distribution was verified by the Kolmogorov-Smirnov (K-S) test. Data were presented as absolute and relative frequency (percentage). Parametric variables were presented as mean and standard deviation of the mean, non-parametric variables were presented as median and variation of the 25th and 75th percentiles. Analyses were performed using the SPSS software version 23.

RESULTS

As described in table 1, the sample consisted of 68 young adults, predominantly males, and of these, 71% were married, most had completed elementary school, 9% reported consuming alcohol, and 12% tobacco during the collection period. Only 7% were tracheostomized, 87% were orally fed, while 13% used a nasogastric tube.

The anatomical region most affected by neoplasms was the oropharynx (69%). All volunteers were irradiated with 2D radiation therapy prior to quality of life assessment. Additionally, 53% of participants underwent surgery and 65% chemotherapy. Of the 65 patients who underwent/ are undergoing chemotherapy, all used cisplatin as an antineoplastic agent.

Table 2 describes the data referring to the assessment of quality of life (UW-QOL). In general, the results suggest a greater impact on the stomatognathic aspects where saliva and taste were the most affected. Most volunteers (66%) reported not being able to swallow some solid foods and 20% reported being able to ingest only liquid foods. Regarding speech, 70% of the sample reported difficulty in pronouncing some words, but still being able to communicate without major problems. A smaller portion (16%) reported being understood only by family and friends.

Regarding the questions aimed at evaluating the activity of daily living, 34% of

patients undergoing chemotherapy reported that they often wanted to go out more, but due to lack of willingness and/or physical conditions, they chose to stay away from recreational activities. The answer to this question should consider the last 6 days prior to the assessment. Moderate pain requiring control by regularly consumed medication was reported by 50% of volunteers. Still, within the subgroup of activities of daily living, when asked about aspects related to shoulder conditions, 56% reported having no problems. A group of volunteers (36%) reported noticing their stiff shoulder, however these volunteers also reported that in their perception of daily activities and strength of the upper limbs remained preserved.

The results obtained from the evaluation of the UW-QOL questions that reflect some aspects of their psychological condition demonstrate, in general, more favorable perceptions in this domain when compared to the first two domains described above. Most volunteers who underwent (65%) or not (67%) chemotherapy did not report feeling anxious about the disease. Humor, for 32% of the volunteers, was rated as excellent, and free from the probable negative interference that cancer could have exerted on this item. Only 11% of the volunteers reported responses compatible with depression associated with the clinical condition involved with cancer.

Table 1 – Clinical and demographic characteristics

Clinical and demographic characteristics	n (%), mean ± SD, median (25-75%)
Male	62 (89)
Age (years)	57,5 ± 8,1
Marital status	
Married	48 (71)
Not married	10 (15)
Divorced	6 (9)
Widowed	4 (6)
Education	
Illiterate	2 (3)
Elementary school (Incomp + comp)	38 (56)
High school (Incomp + comp)	21 (31)
Higher education (Incomp + comp)	7(10)
Neoplastic Location	
Nasopharynx	12 (18)
Oropharynx	47 (69)
Larynx	9 (13)
Chemotherapy	44 (65)
Cisplatin	44 (100)
Surgery	36 (53)
Radiation therapy	68 (100)
RT dose (GY)	67 (60 - 70)
RT Termination Time (months)	5 (3 – 12)
Active Smoker	8 (12)
Active Drinker	4 (6)
Pathway for pulmonary ventilation:	
By tracheostomy	5 (7)
By upper airways	63 (93)

Data are expressed as absolute number (n), percentage (%), mean ± standard deviation of the mean (SD) or as median and interquartile range (25% - 75%). RT = Radiation therapy; GY = Intensity of irradiation expressed in Gray.*

Table 2 – Quality of life assessment: UW-QOL.

Aspects	Median	(25%-75%)
Chewing	50	(50-100)
Swallowing	67	(33-67)
Taste	33	(33-67)
Saliva	33	(33-33)
Speaking	67	(67-67)
Activity	50	(50-75)
Recreation	50	(50-75)
Pain	50	(50-100)
Shoulder	100	(67-100)
Appearance	75	(50-75)
Anxiety	100	(67-100)
Humor	75	(50-100)

Data are expressed as median and interquartile range (25% - 75%). The UW-QOL questionnaire, as described in the methods, assesses quality of life through a graduated scale from zero to one hundred (0-100), where patients are previously instructed to answer a series of questions using progressive numerical identifiers that must be ordered in ascending order when representing a particular clinical condition. Based on this understanding, we can consider that low numbers represent a situation in which the clinical status is unfavorable, while higher numbers represent better health conditions.

DISCUSSION

This study analyzed the quality of life profile at the end of a relatively long period of time after the end of adjuvant radiation therapy used in the antineoplastic treatment of patients with head and neck cancer. It was possible to observe, as expected, that changes in stomatognathic functions predominated as being the most affected

aspects (lowest score on the questionnaire). Changes in speech, chewing, swallowing, and saliva appear as the main changes in the late phase of HNC treatment, and there is strong evidence in the literature pointing to the negative interference relationship that stomatognathic aspects exert on the clinical evolution of these patients, especially in

relation to QoL⁴.

However, the overall score for the aspects of activity, recreation, and pain sensation reached, on average, half of the scaled score in this questionnaire. This is a very important point, as all these variables are within the scope of the rehabilitation objectives. It is possible that the need for chemotherapy, observed in 65% of patients (cisplatin), may have played a major role in the assessment of aspects related to physical performance, since the side effects of this pharmacological treatment involve nausea, vomiting, changes in preferences food, stomatitis, diarrhea, and constipation, which, added to the stomatognathic alterations mentioned above, may have exacerbated the low food intake, consequently leading to a worsening of the nutritional status^{25,26}. Although malnutrition was not evaluated in this study, it is plausible to assume that these patients, due to all that has been discussed so far, need nutritional support, which aims to assess and manage, if any, oncological cachexia. This is a syndrome which originates in a multifactorial manner and is characterized by continuous loss of skeletal muscle mass, worsening functional performance, and may even limit the individual's ability to complete the treatment²⁷.

Another aspect that directly influences the stomatognathic function and may limit the ability of food intake is the appearance of tissue fibrosis induced by radiation therapy²⁸. Symptomatic treatment is common and specific interventions depend on the location and severity of the fibrosis. When fibrosis affects the masticatory muscles, the patient may develop trismus, which will result in reduced jaw mobility, generating a negative impact on nutrition, in addition to causing changes in facial appearance and compromising oral hygiene, among other aspects. Some studies²⁹⁻³¹ report that the prevention of trismus is extremely

important, since radio-induced trismus is difficult to resolve. Studies show that passive and assisted stretching exercises, among other techniques, can significantly increase mouth opening⁷, as well as the importance of performing exercises that act on the mobility of the temporomandibular joint at an early stage. The importance of early onset lies in the growing difficulty in reversing the formation of fibrosis, that is, the protective effects that exercises aimed at increasing/preserving joint mobility decrease over time³². Therefore, early intervention by a physiotherapist and/or speech therapist becomes extremely necessary to prevent or reduce this complication that is so frequent and sometimes overlooked.

Another relevant point is the relationship between chemo-radiation therapy and the significant increase in fatigue, reduced quality of life, and functional capacity³³. Fatigue is one of the most frequent reactions and 63% of patients who use cisplatin and concomitant radiation therapy develop, to a greater or lesser degree, clear signs of low tolerance to effort²¹. In a study that evaluated fatigue, impairment in questions about general activity, humor, usual work, relationship with other people, and enjoyment of life were also identified³³. In this context, physical rehabilitation may be essential in helping to reduce/recover from fatigue.

The implementation of general resistance training has provided good results, especially in motor performance, in the perception of fatigue, in addition to clearly benefiting the results obtained in functional capacity assessment scales, such as the ECOG Performance Status, which can be decisive for the achievement or continuity of treatment³⁴⁻³⁶. However, patients with oncologic cachexia can refuse the proposed conducts in a typical rehabilitation program, as a way to avoid the increase in the

sensation/manifestation of fatigue. Thus, it is important to include exercises that do not require a great deal of energy³⁷. Studies show that interventions with exercises also help to reduce anxiety, depression, sleep disorders, in addition to improving quality of life³⁷.

On the other hand, we observed that 12% of patients reported that they continued to actively smoke at the time of evaluation. Smoking is related to the emergence of several chronic diseases, including chronic obstructive pulmonary disease (COPD)²⁵. Although the experimental design of this study was not structured to assess the implications related to the outcomes of smoking, it is possible to assume, based on scientific evidence²⁵⁻²⁷, that smoking has negatively interfered with physical capacity²⁸. In this aspect, many studies point to the physical limitations imposed by both respiratory changes and other systemic sequelae related to the smoking habit, which can be favorably overcome through pulmonary rehabilitation^{38,39}. Respiratory physiotherapy works by reducing patient discomfort, in addition to decreasing infection rates⁴⁰. This is particularly important, as patients undergoing treatment for HNC have a great potential to develop extensive bronchopneumonia that often evolves into the need for mechanical ventilation and subsequent tracheostomy installation³¹⁻³². Together, these clinical characteristics demonstrate the sensitivity of this quality of life questionnaire (UW-QOL), which is currently considered the main instrument for evaluating patients with HNC. Apparently, with regard to respiratory aspects, which are so relevant due to the region affected by both the neoplasm and the treatments (radiation therapy and surgeries), the clinical information aimed at combating the ventilatory problems imposed by tumor evolution are insufficient to support a more robust analysis.

In contrast, the data from this study revealed that 53% of the participants underwent the surgical procedure. There are many sequelae that can appear in the postoperative period, and many of these sequelae compromise the stomatognathic functions, as mentioned above, but also generate manifestations of pain and limitations of the functionality of the cervical spine and scapular girdle⁴¹. However, this quality of life questionnaire, which is most widely used in the evaluation of patients with HNC, does not address any aspect related to the functionality of the cervical spine. While aspects related to the scapular girdle are summarized in scores directed to the shoulder region where the patients enrolled herein indicated, contrary to expectations, very low occurrences of complaints for this body part⁴².

Finally, even in the face of so many limitations within the global assessment of the possible changes that can be detected in patients undergoing cancer treatment for HNC, the aspects of the quality of life assessment that are related to emotional well-being were, contrary to what expected, the least affected domain. Another study⁴³ found similar results where both mood and anxiety were shown to be, according to the patients' perception, favorable. Perhaps this reflects a certain selection bias, implying that patients who volunteered to participate in these studies have additional motivation to cope with the disease, while patients who chose not to participate in these assessments may have done so precisely because they are not interested in revealing the negative aspects that they are having to daily face while they are moving in the search of a cure for cancer^{44,45}. It is important to emphasize that self-reporting in a broad and generic form is completely different from a psychological assessment designed for this purpose. This implies that the analysis of the volunteers'

perception regarding their psychological state must be carefully interpreted as they are surrounded by very narrow limits regarding the scope of these assessments.

In any case, the simple fact that we found patients who were positive in relation to

emotional and motivational issues reveals a very favorable scenario for the inclusion of rehabilitation proposals, since emotional aspects directly influence both treatment adherence and effectiveness of therapeutic approaches designed to improve functional capacity.

CONCLUSION

As expected, stomatognathic functions were the most affected. However, according to the self-reports collected through the UW-QOL, the low scores observed in the items of pain, activities of daily living, and recreation reinforce the need for a multidisciplinary care approach and, additionally, suggest that there are good

chances that physical rehabilitation would favor the different aspects that constitute quality of life, perhaps altering the clinical course of these unwanted alterations that manifest themselves even after a relatively long period of time at the end of adjuvant radiation therapy used as part of the treatment of HNC.

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