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Frequency of functional and muscular changes after head and neck radiation therapy. A cross-sectional study

Frequência de alterações funcionais e musculares após radioterapia de cabeça e pescoço. Um estudo transversal

DOI:10.34117/bjdv6n7-875

Recebimento dos originais: 03/06/2020
Aceitação para publicação: 31/07/2020

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ABSTRACT

Head and neck cancer is considered a mutilating disease, the therapeutic modalities for treatment include surgical, radiotherapeutic and chemotherapeutic procedures. The aim was to evaluate functional and muscular alterations in the head, neck, scapular girdle and upper extremities of individuals with head and neck cancer after radiotherapy. Cross-sectional study with retrospective data. Seventy-one medical charts were selected, analyzing in each of them the routine of the physiotherapeutic diagnosis of patients that includes information about the disease, physical examination and diagnosis of pain and limitation of movement. The results showed muscular alterations in all patients, most of the changes occurred in the area close to the irradiated site, such as the trapezius (90.1%) and pectoral (80.3%) muscles. All patients underwent radiotherapy, 29 (40.8%) used conventional cobalt therapy and 42 (59.2%) intensity-modulated radiation therapy (IMRT). The most used dose among the patients was 6,300 cGy. The Bisserial Correlation Test showed a correlation between the dose of radiotherapy and the segments: temporomandibular dysfunction, sternocleidomastoid, trapezius, pectoralis, cervical, shoulder, winged scapula, and sensory alterations. Radiation therapy in head and neck cancer causes functional and muscular changes in the irradiated regions. The present study showed that areas that were not directly irradiated should be better studied.

KeyWords: Head and neck neoplasms, Radiotherapy, Physical therapy specialty, Quality of life.

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RESUMO
O câncer de cabeça e pescoço é considerado uma doença mutilante, as modalidades terapêuticas para o tratamento incluem procedimentos cirúrgicos, radioterapêuticos e quimioterápicos. O objetivo foi avaliar alterações funcionais e musculares na cabeça, pescoço, cintura escapular e membros superiores de indivíduos com câncer de cabeça e pescoço após radioterapia. Trata-se de um estudo transversal com dados retrospectivos. Foram selecionados 71 prontuários, analisando em cada um deles a rotina do diagnóstico fisioterapêutico dos pacientes, que inclui informações sobre a doença, exame físico e diagnóstico de dor e limitação de movimento. Os resultados mostraram alterações musculares em todos os pacientes, a maioria das alterações ocorreu na área próxima ao local irradiado, como os músculos trapézio (90,1%) e peitoral (80,3%). Todos os pacientes foram submetidos à radioterapia, 29 (40,8%) utilizaram terapia convencional com cobalto e 42 (59,2%) radioterapia com intensidade modulada (IMRT). A dose mais utilizada entre os pacientes foi de 6.300 cGy. O Teste de Correlação Bisserial mostrou correlação entre a dose de radioterapia e os segmentos: disfunção temporomandibular, esternocleidomastóideo, trapézio, peitoral, cervical, ombro, escápula alada e alterações sensoriais. A radioterapia no câncer de cabeça e pescoço causa alterações funcionais e musculares nas regiões irradiadas. O presente estudo mostrou que áreas que não foram diretamente irradiadas deveriam ser melhor estudadas.

Palavras-Chave: Neoplasias de cabeça e pescoço, Radioterapia, Fisioterapia, Qualidade de vida.

1 INTRODUCTION

Head and neck cancer (HNC) is considered a serious and mutilating disease, in Brazil its incidence is high, causing high rates of morbidity and mortality (LOTHAIRE et al., 2006).

The therapeutic modalities for treatment of head and neck tumors include surgical, radiotherapeutic and chemotherapeutic procedures, which may be used alone or in combination (INCA, 2015; GALBIATTI, 2013). Currently, the most indicated non-surgical treatment is radiotherapy, though this type of treatment can cause acute and chronic adverse sequelae affecting the mouth through the appearance of symptoms such as oral mucositis, reduction of salivary flow, burning of the mouth, radiation cavities, dysphagia, osteoradionecrosis and also generate functional alterations in the muscles of head and neck and temporomandibular joint (STROJAN et al., 2017; ROLIM, COSTA, RAMALHO, 2011; HEIINEN et al., 2016).

The functional alterations most commonly found are trismus, mandibular deviations during movement, pain and limitations in the muscular activities of the head, neck and shoulders, as well as frequent motor and sensory impairment of head, neck and scapular girdle (STROJAN et al., 2017; ROLIM, COSTA, RAMALHO, 2011). These sequelae are not only related to aesthetics, but mainly to vital functions, the patient's ability to communicate, feed themselves, and work-related disabilities (ROLIM, COSTA, RAMALHO, 2011).

The types of head and neck surgeries depend on the tumor location and may or may not be associated with cervical emptying and / or immediate reconstruction. Surgical complications are related to the type of intervention, type of reconstruction and stage of the disease (BAIOCCHI, 2017).

The main complications found in post-surgery patients without cervical emptying are edema, facial paralysis and trismus as a result of surgical extension or adhesions and fibrosis in the cicatricle region (TACANI, 2017). In cervical emptying, in addition to the lymphatic structures, other anatomical structures such as the sternocleidomastoid muscle, the internal jugular vein, the accessory spinal nerve, the superficial cervical plexus and the submandibular gland are also removed. Temporary injury or total resection of the accessory nerve during surgery leads to paralysis of the trapezius muscle causing pain, dropped shoulder, winged scapula, and restriction of shoulder range of motion. Some branches of the cervical plexus may also be resected during cervical emptying, impairing the balance of the glen humeral and scapula-thoracic joints, causing pain and functional impairment (BAIOCCHI, 2017; TACANI, 2017).

Despite studies already conducted on adverse effects of radiotherapy to the mouth, such as xerostomia, mucositis and trismus, for example (HEIINEN et al, 2016; GUSSGARD et al., 2015; GUSSGARD, JOKSTAD, WOOD, HOPE, TENENBAUM, 2015) we have not found in the literature studies that show that the muscular and sensory effects (tingling and sensitive changes) caused only by radiotherapy in the head, neck, scapular girdle and upper limbs can cause further functional alterations, not only in the irradiated tissue, thus influencing body posture and the performance of simple daily activities, which negatively affects these patients' quality of life (STROJAN et al., 2017; ROLIM, COSTA, RAMALHO, 2011; RIGUAL, WISEMAN, 2004; BRADLEY et al., 2011).

The evaluation of muscle and joint sequelae that can happen to patients undergoing radiotherapy is extremely important to prevent sequels and to develop physiotherapeutic treatment protocols, thus promoting increased good quality survival for individuals with head and neck cancer.

2 OBJECTIVES

The objective of this study was to evaluate the muscular and joint functional alterations of the head, neck, scapular girdle and upper limbs of individuals after radiotherapy of head and neck cancer.

3 METHODS

This is a Cross-sectional study with retrospective data from medical records of patients diagnosed with head and neck cancer submitted to radiotherapy. We included in the study all medical records of patients with head and neck cancer who underwent radiotherapy who were attended at the Clinical Research Center of the Bauru School of Dentistry of the University of São Paulo between 2016 and 2017, regardless of whether chemotherapy and/or surgery were performed. We excluded patients from patients who did not undergo physical therapy evaluation or did not present details about the radiotherapy treatment. The consent was obtained for experimentation with human subjects,

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CAAE: 86783118.8.0000.5417. An Ethics Committee, number, endorsed implementation of the study: 2.600.590 on April 16, 2018.

The physical therapy evaluation recorded demographic information such as age, gender and specifics such as primary tumor, type of cancer treatment (radiotherapy, chemotherapy, and surgery), physical examination and pain diagnosis and limitation of motion.

The physical examination reported possible facial asymmetries (eyebrow, ear, nasal wing), as well as temporomandibular joint dysfunctions (TMD) and trismus, alterations of the cervical region (sternocleidomastoid, scalene, trapezius, pectoralis), head (rotation, inclination, forward, increased cervical lordosis), shoulders (elevation, forward, winged scapula, elevated scapula) and upper limbs (sensory and motor alterations).

The examination of pain and limitation of motion evaluated the presence of pain and decreased range of motion in the upper limbs and right and left cervical rotation (RCR and LCR). Therefore, the functional alterations were evaluated through six items: item 1 – facial region, item 2 – cervical region, item 3 – head, item 4 – shoulders, item 5 – upper limbs, item 6 – pain and decreased range of motion, based on Kendal's descriptions, 2007 (KENDAL, 2007).

It is a convenience sample, where all the patients attended during the analysis period participated in the research, so it was not necessary to perform the calculation of the sample.

For the analysis of the results, descriptive statistics was performed in percentages, Fisher's exact test to verify association between radiotherapy and functional changes; association between surgery and functional changes; and association between cervical emptying and functional changes. The Bisserial Correlation Test to verify the correlation between the dose of radiotherapy and the functional changes.

4 RESULTS

From the 71 records selected, 60 (84.5%) were male and 11 (15.5%) were female. Participants ranged from 29 to 87 years old, with median age of 59.9. The most prevalent tumors region were oral cavity with 31 (44%) cases (**Figure 1**).

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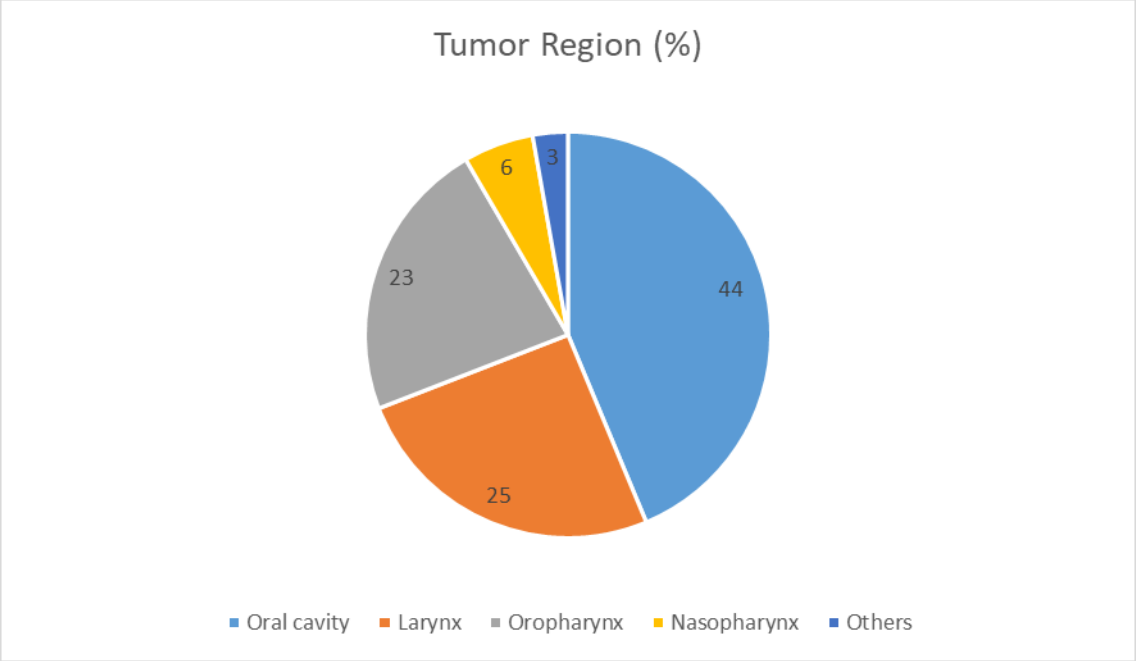
Figure 1 - Region of the tumor among the patients studied



The results showed muscular alterations in all patients, 69 (97.1%) presenting alterations in the facial region, 68 (95.7%) in the cervical region, 60 (84.5%) in the head, 69 (97.1%) in the shoulder region, 41 (57.8%) in the upper limbs, and 28 (39.4%) presenting pain and limitation of motion (**Table 1**).

Table 1 – Functional changes found in participant evaluations

Item 1 Facial region	Radiotherapy N (%)	Radiotherapy and surgery N (%)	Total %
	17 (23,9)	**54 (76,1)**	**100**
Eyebrow	06 (8,5)	29 (40,8)	49,3
Ear	15 (21,1)	37 (52,1)	73,2
Nasal loop (facial mimic)	15 (21,1)	46 (64,8)	85,9
Temporomandibular dysfunction	02 (2,8)	35 (49,3)	52,1
Trismus	09 (12,7)	29 (40,8)	53,5
Total	17 (23,9)	52 (73,2)	**97,1**
Item 2 Neck			
Sternocleidomastoid	15 (21,1)	38 (53,5)	74,6
Scalene	15 (21,1)	53 (74,6)	95,7
Trapeze	14 (19,7)	50 (70,4)	90,1
Pectoral	13 (18,3)	44 (62,0)	80,3
Total	15 (21,1)	53 (74,6)	**95,7**
Item 3 Head			
Rotation	11 (15,5)	48 (67,6)	83,1
Inclination	11 (15,5)	46 (64,8)	80,3
Anteriorisation	09 (12,7)	46 (64,8)	77,5
Cervical lordosis	07 (9,9)	39 (54,9)	64,8
Total	11 (15,5)	49 (69,0)	**84,5**
Item 4 Shoulder			

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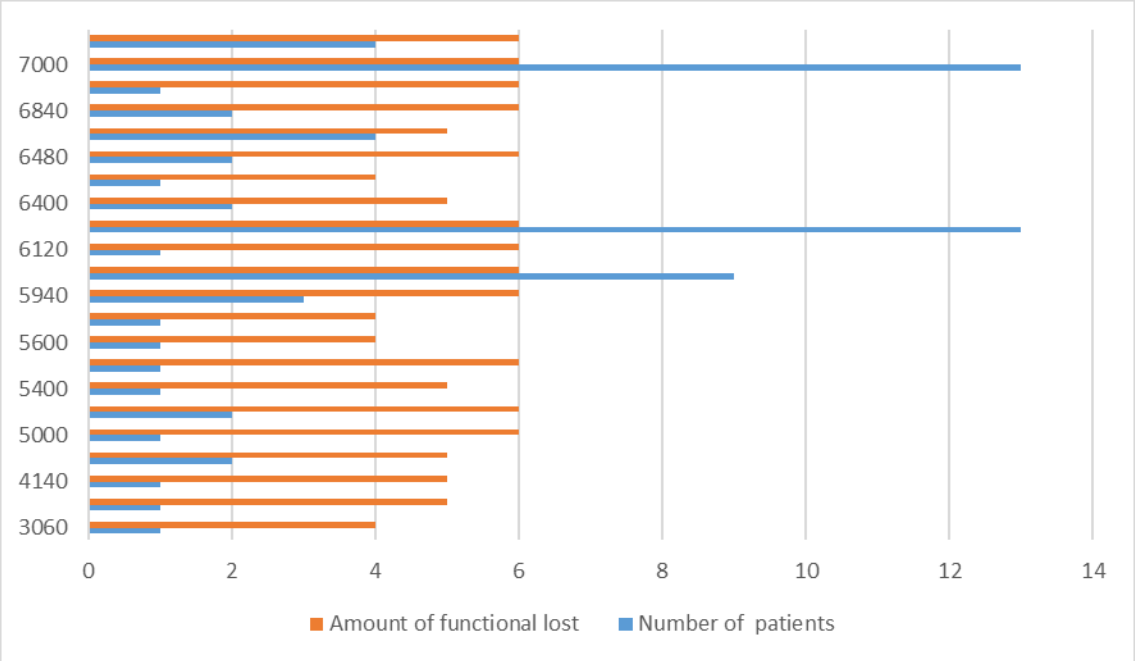
Elevation	11 (15,5)	41 (57,7)	73,2
Anteriorisation	10 (14,1)	47 (66,2)	80,3
Winged scapula	07 (9,9)	39 (54,9)	64,8
Elevated scapula	08 (11,3)	38 (53,5)	64,8
Total	16 (22,5)	53 (74,6)	**97,1**
Item 5 Upper Limbs			
Sensitive alterations	03 (4,2)	32 (45,1)	49,3
Motor alterations	04 (5,6)	23 (32,4)	38,0
Total	06 (8,5)	35 (49,3)	**57,8**
Item 6 Pain and limitation of motion			
Cervical rotation R	03 (4,2)	11 (15,5)	19,7
Cervical rotation L	03 (4,2)	2 (2,8)	7,0
Upper limbs	00 (00,0)	18 (25,4)	25,4
Total	04 (5,6)	24 (33,8)	**39,4**

Regarding the treatment, 50 (70.4%) participants underwent chemotherapy and 54 (76.1%) surgery, and 30 (42.3%) of these patients underwent neck dissection surgery. All patients underwent radiotherapy, 29 (40.8%) used conventional cobalt therapy and 42 (59.2%) intensity-modulated radiation therapy (IMRT). The doses used in the radiotherapy treatment varied between 3,060 cGy and 7,040 cGy, the most used dose among the patients was 6,300 cGy, and all patients presented loss of function through the six items evaluated, regardless of the dosage of radiotherapy (**Figure 2**).

Figure 2 – Radiotherapy doses and amount of functional alterations lost



Fisher's exact test showed an association between radiotherapy and the segments trismus (P= 0, 09), rotation cervical (P=0, 02) and upper limbs (P=0, 05). Association between surgery and the segments rotation cervical (P=0, 03), upper limbs (P=0, 01), temporomandibular disorders (P=0, 01),

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anteriorization cervical (P=0, 01), cervical lordosis (P=0, 03), anteriorization shoulder (P=0, 03), winged scapula (P=0, 03) and sensitive changes (P=0, 05). Association between cervical emptying and the segments anteriorization shoulder (P=0, 03) and sensitive changes (P=0, 01).

The Bisserial Correlation Test showed a correlation between the dose of radiotherapy and the segments: Temporomandibular dysfunction, sternocleidomastoid, trapezius, pectoralis, rotation (cervical), inclination (cervical), elevation (shoulder), winged scapula, and sensory alterations (**Table 2**).

Table 2 - The Bisserial Correlation Test: correlation between dose of radiotherapy and segments

SEGMENTS	r	p
Temporomandibular disorders	- 0,401	0,01
Sternocleidomastoid	- 0,249	0,03
Trapezius	- 0,271	0,02
Pectoralis	- 0, 255	0,03
Rotation (cervical)	- 0,265	0,02
Inclination (cervical)	- 0,345	0,01
Elevation (shoulder)	- 0, 283	0,01
Winged scapula	- 0,361	0,01
Elevated scapula	- 0, 331	0,01
Sensory alterations	- 0, 317	0,01

5 DISCUSSION

Treatment for head and neck cancer can often be as painful and mutilating as the disease itself, leaving psychological, social, and functional sequels. Surgical techniques of tumor removal in the head and neck area may influence the daily activities of the patients, mostly due to the area extension and neck dissection surgery, (RIGUAL, WISEMAN, 2004; BRADLEY et al., 2011), with or without removal of the sternocleidomastoid muscle, jugular vein and accessory nerve, in which cases called modified radical neck dissection surgery (RIGUAL, WISEMAN, 2004; BRADLEY et al., 2011).

In this study, 30 (42.3%) participants underwent neck dissection surgery, but many (95.7%) patients presented disorders of the scalene (95.7%) and trapezius (90.1%) muscles, which may be due to the surgical procedure for tumor removal, the neck dissection itself, or a sequel of the radiotherapy treatment (ZHANG et al., 2015; KIM et al., 2015), since the percentage of patients with disorders in the sternocleidomastoid and trapezius muscles was greater than the percentage that underwent head and neck surgery.

Radiotherapy that affects tissues neighboring the tumor region causes adverse effects, trismus and progressive soft tissue fibrosis of the head and neck region and sub clavicular area, and many patients report feeling a firm tissue that limits motion or causes pain associated to the motion, affecting the functionality of this region (BRAGANTE, NASCIMENTO, MOTTA, 2012; LENNOX et al., 2002). Fibrosis is a pathological process of parenchymal cell damage, stromal remodeling and tissue

contraction. Although fibrosis imitates normal healing, its remodeling phase proves to be uncontrollable. The clinical manifestation of tissue fibrosis presents a reduction of the elasticity and flexibility of the tissue and, depending on its anatomical location, the consequences include tissue distortion, reduction of joint motion, distal lymphedema and, occasionally, neuropathy or pain, and may negatively impact the individual's ability to carry out daily activities, thus affecting their quality of life. Specifically in the head and neck region restriction of mouth opening, shoulder movement, and neck rotation may interfere with feeding, speech, ability to drive, self-care relationship, and occupation (MOLONEY et al., 2015). Radiation in the region of the masticatory musculature, especially in the medial pterygoid muscle and the temporomandibular joint, can cause muscular fibrosis and lead to intense trismus (GRANDI et al., 2007; AL-SALEH et al., 2013; SPEKSNIJDER et al., 2013), which corroborates the results of this study that shows that a high percentage of patients who underwent radiotherapy treatment presented fibrosis-like muscular alterations in the regions exposed to radiation, such as the cervical musculature 68 (95.7%).

Regarding disorders in the shoulder region, studies on radiotherapy damage to this region are relatively rare, and contradictory results are reported on the effects of radiotherapy to the shoulder, as they may be mistaken for the consequences of surgical intervention (SPEKSNIJDER et al., 2013; WATKINS, 2011). In this study, the number of participants who presented alterations to the shoulder due to radiotherapy 69 (97.1%) was greater than the number of patients who underwent surgeries 54 (76.1%), which leads to the hypothesis that the shoulder limitations found specifically in this study were not only caused by surgical interventions but also by radiotherapy, since all patients underwent radiotherapy and most of them, including those who did not undergo surgery, presented some specific alterations in this region of the scapular girdle.

Radiotherapy uses ionizing radiation for the treatment of malignant neoplasms. Basically, there are two types of radiotherapy: teletherapy, also known as external beam therapy because there is a physical distance between the patient and the source of radiation, is done through linear accelerators or cobalt devices; and brachytherapy, which uses radiation sources in direct contact with the tissues (PELISSER et al, 2008). IMRT (intensity-modulated radiotherapy) is a type of external radiotherapy based on advanced linear acceleration for three-dimensional planning and conformal therapy (PELISSER et al, 2008; NUTTING et al., 2009). In treating head and neck cancer, IMRT allows greater preservation of structures, such as parotids, mucosa of the upper digestive tract, optic nerves, cochlea, pharyngeal constrictors, encephalon and spinal cord. This therapy also allows the preservation of adjacent tissues and increased doses in some tumors, since neighboring tissues are little affected. Currently, most radiotherapy centers in the world have IMRT. In Brazil, it is not widely

used due to the high cost, so it is available only in a few centers in the country (NUTTING et al., 2009; KONG et al., 2016).

Treatment using IMRT is more effective in preserving neighboring structures, thus causing fewer unwanted side effects (NUTTING et al., 2009; SAMUELS, FREEDMAN, ELSAYYAD, 2016). In this study, no significant differences were observed between the type of radiotherapy used and the number of muscle functions lost, since the two types of treatment (IMRT and cobalt therapy) were associated with great movement limitations, and no significant differences were observed among the dosages of radiotherapy. The literature shows these differences for oral sequels, such as hypo salivation and oral mucositis (LOORENTS et al., 2016; SANGUINETI et al., 2015). However, no study has yet evaluated the same functions proposed in this study and compared the two types of treatment (IMRT and cobalt therapy). The epidemiological design of this study does not allow us to state whether or not there is a difference between the radiotherapy methods as regards the loss of the functions evaluated. Therefore, prospective longitudinal studies with a greater number of participants are necessary to reach a conclusion on this aspect.

Functional alterations in the head, neck and scapular girdle regions were evaluated in individuals who underwent radiotherapy after head and neck cancer, but no literature was found on this specific topic. Studies have shown functional alterations in the shoulder and scapular girdle resulting from cases of surgery, with and without neck dissection, and decreased muscle strength and fibrosis due to radiotherapy in the cervical region, leading patients to dysphagia, which is not in line with our evaluation proposal (SUN et al., 2015; RUSSELL, CONNOR, 2014). Regarding radiotherapy, we have only found articles reporting trismus resulting from radiotherapy in the region of masticatory muscles and/or temporomandibular joint,[4] but no reports of possible functional alterations in non-irradiated regions, such as trapezius and pectoralis. Therefore, the results of the literature differ greatly from those found in this study.

Due to the close relation between the muscles of the head and the cervical region with the stomatognathic system, postural deviations can occur in the head and body (SUN et al., 2015; RUSSELL, CONNOR, 2014; BASSO, CORRÊA, SILVA et al., 2010). Therefore, the radiotherapy performed in this region may, in some way, in addition to causing fibrosis and decreased functionality in the temporomandibular joint and masticatory muscles, also be related to important functional alterations in body structures that were not directly affected by the radiotherapy, such as cervical region, shoulder, scapular girdle and upper limbs, which explains the results of this study, where many participants showed loss of function not only in the irradiated regions, but also in regions that were not the focus of the radiation, such as trapezius 64 (90.1%) and pectoralis 57 (80.3%).

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Statistical analysis showed, through Fisher's exact Test, an association between radiotherapy and segments: trismus (P = 0.09), cervical rotation (P = 0.02) and upper limbs (P = 0.05); association between surgery and segments: cervical rotation (P = 0.03), upper limbs (P = 0.01), temporomandibular disorders (P = 0.01), forward neck (P = 0.01), cervical lordosis (P = 0.03), forward shoulder (P = 0.03), winged scapula (P = 0.03) and sensory alterations (P = 0.01); and association between neck dissection and segments: forward shoulder (P = 0.03) and sensory alterations (P = 0.01).

The trismus can be induced by radiotherapy, since it causes fibrosis of the musculature affected by the radiation that normally reaches the masticatory muscles (STROJAN et al., 2017), and the limitation of cervical movements can occur when the radiation focuses this region, reaching the sternocleidomastoid muscle, in the cases of nasopharyngeal carcinoma, for example. Radiation in the cervical region can cause atrophy over time, and the degree of atrophy is associated with cervical weakness, which may explain the results of this study (ZHANG et al., 2015). There are both sensory and motor alterations in the upper limbs and shoulder in patients who underwent neck dissection surgery, regardless of radiotherapy. Therefore, the hypothesis found in this study that only radiotherapy can cause changes in the upper limbs deserves further research.

Patients who undergo antineoplastic treatment, which includes both radiation therapy and neck surgery and dissection, develop postural abnormalities induced by contractures and tissue fibrosis, muscle atrophy and generalized weakness. With these progressive postural changes, individuals may develop loss of anterior pectoral muscle function, resulting in marked kyphosis and rectification of lumbar lordosis, protrusion of the head and internal rotation of the humeral region, which corroborates the findings of this study (MURPHY BA, 2015; GHIAM et al., 2017).

Bisserial Correlation showed inversely proportional correlations between radiotherapy dose and segments: temporomandibular disorders (P=0.01), sternocleidomastoid muscles (P = 0.03), trapezius (P = 0.02) and pectoralis (P = 0.03), (cervical) rotation (P = 0.02), (cervical) tilt (P = 0.01), elevation (shoulder) (P = 0.01), winged scapula (P = 0.01), elevated scapula (P = 0.01) and sensory alterations (P = 0.01). The analysis, because it is inversely proportional, leads us to the result that the greater the dose of radiotherapy received by the patients, the lower the disorders found in the segments. It was observed, however, that the patients who received the highest doses of radiotherapy were those who did not undergo any surgery. Radiotherapy interferes negatively in the functional loss of irradiated regions (BRAGANTE, NASCIMENTO, MOTTA, 2012), so patients receiving higher doses of radiotherapy in this study showed less functional loss not because radiotherapy does not influence this loss, but because these patients were compared with patients who, in addition to receiving radiotherapy treatment, also underwent tumor removal and neck dissection surgery, which

is an extremely mutilating treatment that brings many functional sequels. There is, therefore, the hypothesis that functional losses in irradiated and non-irradiated regions may be greater when the surgical treatment is done together with the radiotherapy, compared to the radiotherapy alone, regardless of the dosage used.

Given that there is a close relation between muscle chains (SUN et al, 2015) and a muscle that shows loss or decrease in functionality may negatively influence other muscles, further research is needed to evaluate the functional alterations in patients who underwent head and neck radiotherapy.

The main limitation of the present study was the type of epidemiological design that did not allow us to conclude cause and effect relationships. Another limitation of this study was the difficulty of comparing our results with the current literature, since it is a subject that although it is very important because it shows us the implications that the antineoplastic treatment can bring to the musculoskeletal structures, is still little explored

6 CONCLUSION

Radiotherapy treatment specific for head and neck cancer causes functional and muscular alterations in the irradiated regions, such as the masticatory muscles, temporomandibular joint and cervical region. Cobalt therapy and IMRT showed loss of function regardless of the dosage used. There are functional alterations in regions that were not the focus of the radiation, such as trapezius and pectoral muscles and scapular girdle.

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