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TREATMENT OF LARYNGEAL AND HYPOPHARYNGEAL CANCER IN THE ELDERLY FROM THE AGE OF EIGHTY

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ABSTRACT

Introduction: Characteristics of the Brazilian population have been changing in the recent decades. A growth of the senior population since the eighties has resulted in alteration in the incidence of the diseases and mortality. **Objective:** to study the epidemiological and prognostic factors and predictive responses of squamous cell carcinoma of larynx or hypopharynx treated in patients with 80 years or older. Methods: a retrospective study analyzed the medical records of 38 patients with 80 years or older treated for larynx or hypopharynx cancer at the National Institute of Cancer, Rio de Janeiro, (INCA/MS) between January 2015 and December 2018. Gender, age, stage, treatment carried out and the patients' clinical evolution were analyzed. For the statistical analysis, the p value was considered significant when smaller than 0.05, when calculated by the qui-square method and the regression of Cox. The survival curves were analyzed by the Kaplan-Meyer method. **Results:** twenty-seven elderly patients with larynx cancer and 11 with hypopharynx cancer were included, being 26 (68.4%) men and 12 (31,6%) women. The mean age was 84.8 years (80 to 94 years). Seventy-nine percent of patients had stages III or IV of disease. Eighteen patients (47.4%) were treated, 6 (15.8%) underwent surgery at some point of the treatment. Twelve patients (44.4%) were treated by exclusive radiation therapy, with an average dose of 51.4 Gy (6–70 Gy). Complete response of treatment was achieved in 13 cases (48.1%), eight of them treated solely by radiation therapy, 3 by surgery alone and 2 by surgery combined with radiotherapy. The incidence of recurrence was 26.3% (10 cases) and death occurred in 24 cases (63.1%). The mean disease-free survival was 11 months, and mean overall survival was 10.3 months. The most important prognostic factors to increase mortality were the tumor size ($p = 0.04$) and stage of disease ($p = 0.03$). No difference in survival was noted comparing treatment modalities ($p = 0.53$). **Conclusion:** the most important prognostic factors to increase mortality were tumor size ($p = 0.04$) and stage of disease ($p = 0.03$). There was no variable evidence of prognostic impact in recurrence of the disease. Treatment modality in this group of patients showed no difference in disease-free survival and overall survival.

INTRODUCTION

The increase in life expectancy has entailed growth in the senior population in our country. In the early 1980´s, the number of people older than 80 years old was of 590,968. In the 2016 Brazilian population census, the population of the aforementioned age group reached 3,458,279 people[1]. As a consequence of this demographic change, the incidence and mortality rates of different diseases in the population have been altered. Old age is one of the greatest risk factors for neoplastic diseases. Half of them become clinically evident in people older than 70[2] years. Head and neck cancer are no different and tend to show in senior patients. Due to the lower life expectancy rates of this age group compared to younger patients, the benefits of radical treatments in senior patients for neoplastic diseases are questionable. One of the greatest challenges is to identify how much the patient can benefit from treatment.

The objective of this work is to study epidemiological characteristics, treatment, and prognosis of eighty-year-old or older patients with larynx and hypopharynx cancer.

PATIENTS AND METHODS

A retrospective study was developed through the analysis of 27 medical records of 80-year-old or older patients treated for larynx and hypopharynx cancer at the

National Institute of Cancer in Rio de Janeiro (INCA-RJ/MS) between January 2015 and December 2018. Gender, age, stage, presence of comorbidity, primary tumor location, treatment carried out, and clinical evolution of patients were analyzed. The statistical study was performed through the Epi-Info 2002 software, which considered p significant when smaller than 0.05. The survival curves were analyzed through the Kaplan-Meyer method, and compared through the log rank test.

RESULTS

Twenty-seven senior patients aged 80 years old or older with larynx cancer and 11 with hypopharynx cancer were treated. Twenty-six patients (68.4%) were men and 12 (31.6%) were women. The histological type, in all cases, was squamous cell carcinoma, being 35% of cases (92.1%) moderately differentiated, and, in three cases (7.9%), poorly differentiated. Twenty (74%) patients smoked and 14 (51.8%) consumed alcoholic beverages**.**

The mean age was of 84.8 years old (81 – 90 years old), being most of them (25 – 65.8%) aged between 80 and 85 years old. Ten patients (26.3%) were aged between the range of 86 and 90 years old, and three (7.9%) were older than 90 years old.

Most patients presented an advanced stage due to local or regional advanced disease. There were no cases of distant metastasis at the moment of registration (tables 1 and 2).

Twelve (31.6%) patients presented comorbidity. Ten (26.3%) were considered unsuitable for therapeutic possibilities before starting any type of curative treatment, and 10 other patients (26.3%) were not treated despite of the therapeutic indication. Among 18 (47.4%) patients treated, six (15.8%) underwent surgery at some point during treatment, being adjuvant radiation therapy used in 2 (5.3%) of them. Radiotherapy was the exclusive modality of treatment used in 12 cases (31.6%). The average dose of radiation therapy was of 60Gy, varying from 50 to 70Gy. The complete response to treatment was reached in 13 cases (72.2% of treated patients), being the exclusive therapeutic modality in eight (61.5%) of them.

The incidence of recurrence was of 26.3% (10 cases), being local in eight cases (80.0%), distant (lung) in one case (10.0%), and regional in another case (10.0%). Among nine patients treated who presented a local recurrence, seven had been treated solely with radiation therapy, one with surgery, and one with surgery combined with radiotherapy.

The mean disease-free survival was of 11 months. There was no significant statistical difference when the disease-free survival was compared to the type of treatment chosen (log rank = 0.66).

Death occurred in 24 cases (63.1%) and, in more than 90% of cases, it occurred due to the oncological disease. The average global survival was of 11.6 months.

There was no significant statistic difference when comparing the global survival to the type of treatment carried out and the group of patients Who were not submitted to any type of treatment (log rank = 0.53).

No variable presented significant statistic relation when compared to the remissive (table 3). Smaller tumors (p = 0.04) and sick patients in earlier stages of the disease (p = 0.03) were related to the statistical significance with lower mortality rates. The type of treatment used did not alter mortality levels (table 4).

DISCUSSION

The growth of the senior population in our country has created a higher interest in the study of differentiated behavior of neoplastic diseases and different therapeutic responses. The development of cancer in patients aged 40 or below is uncommon. The risk increases drastically among patients aged 60 and 70[3]. The occurrence of cancer in senior patients is frequent and growing. However, it is still not studied enough[4] and has become an emergency issue.[5]

There is a difference between biological and chronological ages in several patients, which allows a 70-year-old patient to present better cardiovascular or breathing conditions than a 60-year-old one. Therefore, the treatment in senior patients must be individualized, respecting each patient's characteristics.[3] In an attempt to reduce this bias, it was opted to study patients aged 80 or older, due to the improbability of having oncological patients with functional reserves similar to patients 10 or 20 years younger.

A large number of studies opts to consider senior patients those aged 70 years old or older. In our group, the age range was between 80 and 94 years old, with mean age of 84.5 years old. In the United States, people aged 65 years old have, in average, a life expectancy of another 16 years (women: 19 years, men: 17 years). When they get to the age of 85, this expectancy is lowered to 6 years.[6] It is important to consider the benefits of submitting a patient with a short life expectancy to a treatment that may alter significantly their quality of life.

A very important characteristic of the oncological disease in seniors and that, for the most part is crucial when choosing the appropriate therapeutic option, is the stage in which the disease is at. Cancer in geriatric patients is usually diagnosed at an advanced stage.[7] The interaction between the age of patients and the treatment for neoplastic diseases is widely discussed. In elderly patients, the chance of an inappropriate treatment, i.e., less radical than it should be, makes these patients' prognosis poorer due to the low control of the cancer.

The individualization of treatment is pivotal in the approach of the oncological disease in senior patients[8], since this group does not necessarily present a poorer prognosis than the younger age groups[9] nor any difference in quality of life and surgical or clinical complication rates.[10]

The largest tumor size (p = 0.04), the most advanced stage of the disease (p = 0.03), and the absence of comorbidities were the variables that presented statistical significance when related to mortality levels.

The presence of lymphatic metastasis is a factor of the worst prognosis for the recurrence of the disease. In this study, the presence of lymphatic metastasis and any other variable studied were not related to the remissive of the disease. Surgery did not improve global survival levels.[11] Among then 27 patients aged 80 or older, there was no difference in the mortality levels according to the type of treatment, whethermsome type of treatment had been used or not.

Table 1 – Senior patient stage (≥ 80 years old) treated for larynx cancer.

Stage							
T		N			M		
T1	5	13.1% N0	23	60.5%			
T2	8	21.0% N1	6	15.8%	M0	38	100%
T3	18	47.5% N2	7	18.4%	M1	0	0%
T4	7	18.4% N3	2	5.3%			
Total	38	100% Total	38	100% Total	38	100%	

Table 2 – Senior patient stage (≥ 80 years old) treated for larynx cancer.

Stage	No. of patients	%
I	3	7.9
II	5	13.1
III	17	44.8
IV	13	34.2
Total	38	100

Table 3 – Univariate analysis comparing the tumor size (T), lymphatic metastasis (N), stage of the disease (E), age of patients, gender, and treatment used with the remissive of the disease in senior patients (≥80 years old) treated for larynx and hypopharynx cancer who were treated and presented a complete response to treatment.

	Remissive			
	yes	no	total	p
T				
1	1	1	2	
2	3	0	3	0.64
3	6	1	7	
4	0	1	1	
N				
0	7	2	9	
1	2	1	3	1.0
2	1	0	1	
3	0	0	0	
Stage				
I	1	1	2	
II	3	0	3	0.78
III	5	1	6	
IV	1	1	2	
Gender				
female	4	0	4	0.54
male	6	3	9	
Comorbidity				
No	4	3	7	0.24
Yes	6	0	6	
Age				

Table 4 – Uni and multivariate analysis comparing the tumor size (T), lymphatic metastasis (N), stage of the disease (E), age of patients, gender and treatment used with the incidence of death in senior patients (≥ 80 years old) treated for larynx and hypopharynx cancer.

	Death			
	yes	no	total	p univariate/ multivariate
T				
1	1	4	5	
2	4	4	8	0.04 / 0.09
3	14	4	18	
4	5	2	7	
N				
0	13	10	23	
1	5	1	6	0.34
2	4	3	7	
3	2	0	2	
Stage				
I	0	3	3	
II	1	4	5	0.03 / 0.15
III	14	3	17	
IV	9	4	13	
Gender				
female	6	6	12	0.43
male	18	8	26	
Comorbidity				
No	20	6	26	0.2

CONCLUSION

The main prognosis impact factors for mortality were the size of the tumor (p = 0.04) and the stage of the disease (p = 0.03). However, more than 70% had the disease diagnosed on stages III and IV, which resulted in a poor prognosis. No variable presented prognosis impact for the remissive of the disease. There was no difference in the survival curve related to the type of treatment chosen (p = 0.53).

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