ejpmr, 2019,6(2), 136-140

SJIF Impact Factor 4.897

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

TREATMENT OF HEAD AND NECK CANCER IN THE ELDERLY FROM THE AGE OF EIGHTY

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Article Received on 05/12/2018 **Article Revised on 26/12/2018** **Article Accepted on 17/01/2019**

ABSTRACT

Introduction: Brazilian population characteristics have been changing in the last decades. Senior population has been growing since the 1980s, resulting in changes of incidence and mortality rates. **Objective:** To describe the epidemiologic characteristics and prognostic factors of disease-free survival and overall survival in patients older than 80 years of age with head and neck cancer. **Patients and methods:** A retrospective study of 142 patients older than 80 years of age with head and neck cancer treated in the National Cancer Institute, Rio de Janeiro, Brazil (INCA-MS-RJ). Gender, age, stage, associated diseases, primary tumor site, treatment and outcome of the patients were analyzed. Statistical analysis was made considering the level of statistical significance when $p < 0.05$, using x2 test for univariate analysis and Cox regression for multivariate analysis. The analysis of the survival rate curves was performed with the Kaplan-Meyer method and compared with log rank test. **Results:** One hundred forty-two patients were studied, being 74 women (45%) and 78% men (55%). The mean age was 84.5 years (range, 80 – 94 years). The mouth was the most frequent site of the primary tumor, followed by oropharynx, larynx and hypopharynx. Most patients were in stage III (44 cases, 30.1%) and IV (64 cases, 45%). The squamous cell carcinoma was the most frequent histological type (93%). Thirty-four patients (23.9%) were not treated because they were not suitable for therapeutic approach. The most frequent treatment was the radiation therapy, with mean radiation dose of 51.4 Gy (6 – 70 Gy). We did not find any prognostic factor that could have influenced in disease-free survival. Maxillary sinus and hypopharynx tumors, advanced stage of disease, and the type of treatment performed had relationship with the increasing of mortality rates. Eighty-two (57.7%) patients died during the period of study. The mean disease-free survival was 11.93 months, and the mean overall survival was 16.18 months. **Conclusion:** The largest part of elderly people has oncologic disease detected in advanced stages (stages III and IV). No prognostic factor that could have influenced in disease-free survival was found. Maxillary sinus and hypopharynx tumors, advanced disease, and surgery combined with radiation therapy treatment were linked with increasing mortality rates. Increasing in survival was not observed with different types of treatment (surgery, radiation therapy or combined treatment), unless in early tumors, in which the radical treatment is more recommended.

KEYWORDS: Maxillary sinus and hypopharynx tumors.

INTRODUCTION

Demographic characteristics of the Brazilian people have changed in the past decades. Due to the increase in life expectation, there has been a growth in the senior population in our country. In the early 1980s, there were 590,968 Brazilians older than 80 years. In the 2016 Brazilian population census, the population of the aforementioned age group was of 3,458,279 people.[1]

Old age is one of the greatest risk factors for neoplastic diseases. Half of them becomes clinically evident in people older than 70 years.[2] Head and neck cancer are no different and tend to strike 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 are questionable. One of the greatest challenges is to identify how much the patient will benefit from treatment.

The possibility of a better understanding of evolution and prognosis of the oncological disease in senior patients brings about the necessity to study cancer in this population. It seeks to identify criteria that enables the choice of the best therapeutic option since a more radical treatment will not necessarily alter the survival curve.
Our objective was to study epidemiological characteristics, treatment, and prognosis of 80 year-old or older patients with head and neck tumors.

PATIENTS AND METHODS

A retrospective study was developed through the analysis of 142 medical records of 80-year-old or older patients treated for head and neck cancer at the National Institute of Cancer, Rio de Janeiro, Brazil (INCA/MS), for a period of two years.

Gender, age, stage, presence of comorbidity, primary tumor location, treatment used, and clinical evolution of patients were analyzed.

The statistical study was performed considering p significant when smaller than 0.05 in the qui-square and Cox regression for univariate and multivariate analysis, respectively. The survival curves were analyzed through the Kaplan-Meyer method, and compared through the log rank test.

RESULTS

For a period of two years, 142 patients were registered in the Head and Neck Surgery Section at the National Institute of Cancer (INCa/MS). Sixty- four (45%) were women and seventy-eight (55%) were men. The mean age was 84.5 years, ranging from 80 to 94 years old.

The most frequent tumor location was the oral cavity (57 – 40.2%), followed by the oropharynx (30 –21.2%), larynx (27 – 19%), hypopharynx (11 – 7.7%), maxillary sinus (10 – 7.0%), parotid gland (3 – 2.1%), nasal cavity (2 – 1.4%), skin (1 – 0.7%), and rhinopharynx (1 –0.7%). Most patients arrived at the institution in advanced stages. More than half of patients arrived on stage III (44 cases – 30.1%) and stage IV (64 cases – 45.0%) – table 1.

The epidermoid carcinoma was the histological type found in 132 patients (93%), being the most frequent in the group of senior patients studied. The other 7% were two lymphoma cases, two sarcoma cases, one adenoid cystic carcinoma case, one acinar cell carcinoma case, one mucoepidermoid carcinoma case, one undifferentiated malignant neoplasm case, one oat cell case, and one adenocarcinoma case.

Comorbidity was present in 48 (33.8%) of patients, being the systemic arterial hypertension the most frequent entity (37 – 26%), followed by chronic obstructive pulmonary disease (8 – 5.6%), coronary artery disease (7 – 4.9%), congestive heart failure (7 – 4.9%), Diabetes Mellitus (6 – 4.2%), and cerebrovascular accident (2 – 1.4%). Some patients presented a combination of diseases.

Thirty-four patients (23.9%) were considered unsuitable for therapeutic possibilities before any type of surgical, radiotherapeutic, or chemotherapeutic treatments. The oncological disease treatment was performed in 80 patients (56.3%), being exclusive radiation therapy the most frequent treatment. It was applied in 47 patients (33.1%), with an average dose of 51.4 Gy (6 – 70 Gy), followed by surgery (17 – 12%), surgery and adjuvant radiotherapy (15 – 10.6%), and chemotherapy in only one patient (0.7%).

Table 1 – Relation between the tumor location and senior patient stages (! 80 years) treated at the Head and Neck Surgery Section at INCa, from January 2015 to December 2018.

	Tumor Location									
Stage	mouth	nasal cavity	hypopharynx	larynx	oropharynx	parotid	skin	rhinopharynx	maxillary sinus	Total
I	5	0	1	2	2	0	0	0	0	10
II	11	0	0	5	7	0	0	0	0	23
III	16	0	6	11	10	0	0	0	2	45
IV	25	2	4	9	11	3	1	1	8	64
Total	57	2	11	27	30	3	1	1	10	142

Twenty-six patients (32.5% of patients treated) responded completely to the treatment proposed, and 16 (61.5%) among those presented recurrence of the disease throughout the follow-up period. There was no significant statistic relation when the location or stage of the disease, gender, presence of comorbidity, and type of treatment used were compared to the recurrence rates (table 2).

Eighty-two patients (57.7%) progressed to death, in which 89.2% of cases death occurred due to the oncological disease, and in 10.8% it was due to other diseases (respiratory infections, cardiopathy, sepsis).

Except for patients who were considered unsuitable for therapeutic possibilities before any type of traditional treatment, the average disease-free survival was of 11.93 months and the global survival was of 16.18 months.

DISCUSSION

The growth of the senior population in our country has created a higher interest in the study of the differentiated behavior of neoplastic diseases and different therapeutic responses. The development of head and neck cancer in patients aged 40 or below is uncommon. This risk

drastically increases between 60 and 70 years old patients. The occurrence of cancer, in senior patients, is more and more frequent. However, it is yet not studied enough and has become an emergency issue.[3]

The disease-free survival curves comparing types of treatments used did not present significant difference (Figure 1).

From 142 patients analyzed, 82 (57.7%) progressed to death during the study period. In the univariate analysis, the tumor location (hypopharynx and maxillary sinus tumors) (p = 0.0001), the most advanced stage of the disease (p = 0.0001) and the treatment performed (surgery combined with radiotherapy) (p = 0.01) were factors that had prognosis impact on mortality rates of this group of patients. However, in the multivariate analysis, neither of these variables presented statistical significance (table 2).

When the global survival curves of the patients of this study were analyzed, it was possible to observe that patients treated solely with radiotherapy or combined with surgery displayed a longer survival (Figure 2).

Table. 2: Univariate analysis comparing the location and stage of the disease (E), presence of comorbidity, gender, and treatment performed to the recurrence of the disease in senior patients (! 80 years) treated for head and neck cancer, and who responded completely to treatment at the Head and Neck Surgery Section at INCa, between January 2015 and December 2018.

	Remissive			
Location	yes	no	total	p
Mouth	4	4	8	
Oropharynx	7	3	10	
Larynx	3	2	5	0.59
Hypopharynx	1	0	1	
Maxillary Synus	0	1	1	
Parotid	1	0	1	
Comorbidity				
Yes	8	2	10	0.26
No	8	8	16	
T				
1	2	1	3	
2	4	3	7	0.73
3	9	4	13	
4	1	2	3	
N				
0	9	7	16	
1	4	3	7	0.34
2	3	0	3	
Stage				
I	0	1	1	
II	2	2	4	0.50
III	9	4	13	
IV	5	3	8	
Gender				
female	8	3	11	0.55
male	8	7	15	

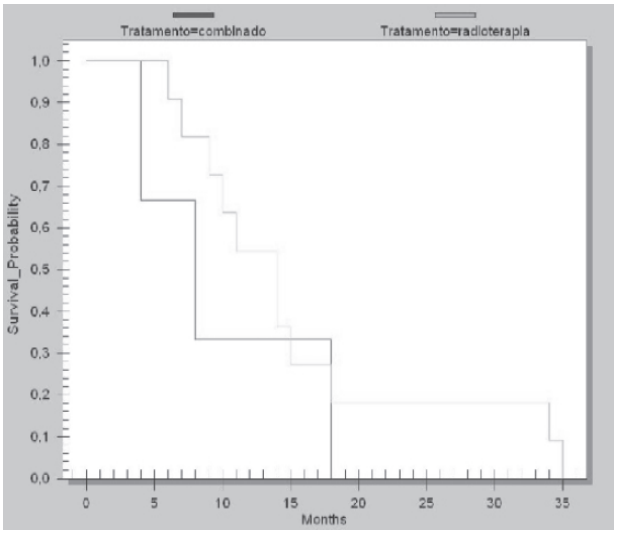

Figure. 1: Disease-free survival curve graph, according to the type of treatment used in senior patients (! 80 years) treated for head and neck cancer and who responded completely to treatment at the Head and Neck Surgery Section at INCa, between January 2015 and December 2018.

og rank: 0.39; Combining: Surgery + Radiotherapy

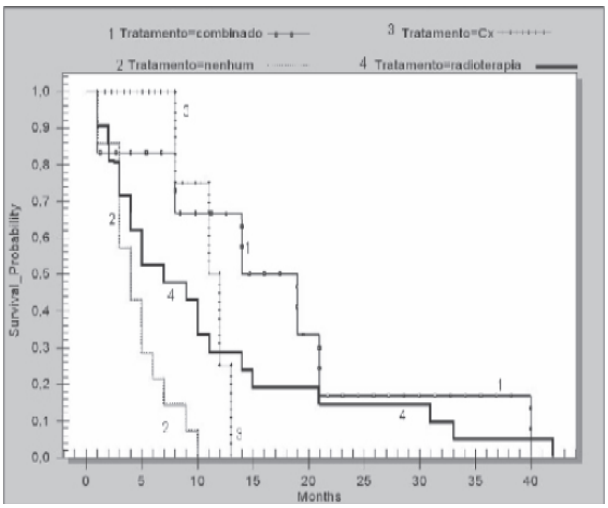

Figure. 2: Global survival curve graph according to the type of treatment used in senior patients (! 80 years) treated for Head and Neck Cancer at the Head and Neck Surgery Section at INCa from January 2015 to December 2018.

Log rank: 0.04; Cx: Surgery; Combining: Surgery + Radiotherapy

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. 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 opt to consider senior patients those aged 70 years old or older. In our group, the age range of patients varied between 80 and 94 years old, with an average of 84.5 years old. In the United States, people aged 65 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 years4. It is at this point that the benefits of submitting a patient with a reduced life expectancy to a treatment that may significantly alter their quality of life should be assessed.

The incidence of comorbidity in the geriatric group is very different when compared to younger groups of patients. More than a third of patients with cancer present, at least, one comorbidity, being systemic arterial hypertension the most common one, which occurs in more than half of patients with cancer and older than 70 years old5. The same happened in our group of patients. Systemic arterial hypertension was present in 37 (26%) patients with cancer treated in our facility. Chronic obstructive pulmonary disease was diagnosed in only 8 patients (5,6%), despite the high rate of smokers in our study, being 102 (71.8%) in total. Even though the role of smoking in the carcinogenesis of head and neck cancer has been defined, this relevance decreases in the group of patients with more advanced age.[5,6]

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 more advanced stages[7], perhaps due to the low acknowledgement of complaints in this group of patients. Over 75% of patients analyzed in this study were diagnosed with stages III and IV cancer, which influenced the therapeutic choice and the prognosis of any patient and any age range.

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.

There is much prejudice about the cancer treatment in elderly patients: 1 – this group does not have the same functional capacity to endure surgical, chemotherapeutic, or radiotherapeutic treatment; 2 – global survival will not be determined by neoplastic disease, but by the patient's comorbidity and global health condition; and 3 – senior patients have less aggressive oncological diseases.[8]

Several studies made a relation between patient's clinical conditions, tumor stage, and the type of treatment to the therapeutic response, free of disease and survival time. There was no statistical difference between the younger and the senior group of patients.[6,9-12]

Only a little more than half of the group (56.3%) underwent some type of treatment with curing intent. Less than 20% of patients presented a complete response to the lesions of the treatment proposed and, in this small group, recurrence of the incidence of the disease was very elevated, reaching 61.5%. The recurrence of the disease was not related to any of the variable studied with statistical significance, maybe due to the small number of patients who presented a complete response to treatment and who may present a recurrence of the disease during the follow-up period.

When analyzing a larger group of patients, it was noted that patients at a more advanced stage of the disease (stages III and IV) presented a higher rate of death ($p = 0.0001$), which is a result commonly found in any type of tumor and at any age range studied. The mortality was also higher in the group treated with surgery combined with radiation therapy, and in patients treated for hypopharynx and maxillary sinus cancer,respectively, 90.9% and 100% of patients progressed to death.

Both the hypopharynx and the maxillary sinus tumors are responsible for oligosymptomatic clinical states or misinterpreted symptoms, and are, usually, followed by a late diagnosis, which decreases the therapeutic response and increases mortality.[13]

Patients who underwent isolated radiotherapeutic or treatments combined with surgery presented a higher global survival when compared to patients who solely underwent surgical treatment, or the group of patients who did not undergo any type of treatment with global survival rates respectively of 28%, 68%, 25%, and 0% in 12 months (figure 2). By the end of 24 months, no patient solely treated with surgery or that had not undergone treatment was alive. The survival, in this period, of patients treated with radiation therapy and surgery combined with radiation therapy decreased to 15% and 18%, respectively. Clayman et al. described a global survival, in patients older than 80 years old treated surgically for head and neck cancer, near to 70% in 12 months, lowering to 50% in 36 months.[14]

The individualization of treatment is pivotal in the approach of the oncological disease in senior patients17, since this group of patients does not necessarily present a poorer prognosis than the younger age groups[15] nor any difference in quality of life and surgical or clinical complication rates.[16]

The high rate of patients who were not submitted to any type of treatment, associated with a higher mortality rate in T3 and T4 patients, and in stages III and IV patients, showed the importance of an early diagnosis. The treatment becomes more effective and offers less morbidity for the patient, being more tolerated in the group of senior patients.

CONCLUSION

One hundred and nine (76.8%) patients had a more advanced stage of neoplastic disease diagnosis (stages III and IV). No variable studied presented a relation with the remissive of the disease in this group. Patients treated for hypopharynx and maxillary sinus tumor (p = 0.0001), larger tumor size (p = 0.0006), more advanced stages of the disease (p = 0.0001), and treated with radiation therapy and surgery combined with radiotherapy (p = 0.01) presented a higher rate of mortality. The mean disease-free survival was of 16.1 months. There was no difference in survival according to the type of treatment given.

The data in this study show the importance of early diagnosis in neoplastic diseases, for it enables a more effective radical treatment, when treated at early stages, with better oncological control and less morbimortality, being therapy indicated for any patient, regardless of their age range.

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