

COMPARISON OF TREATMENT USING TELETERAPY (EXTERNAL BEAM RADIATION) ALONE VERSUS TELETERAPY COMBINED WITH BRACHYTHERAPY FOR ADVANCED SQUAMOUS CELL CARCINOMA OF THE ESOPHAGUS

Comparação dos tratamentos do carcinoma espinocelular avançado do esôfago pela teleterapia exclusiva e pela teleterapia associada à braquiterapia

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ABSTRACT - Background - Squamous cell carcinoma of the esophagus is still a difficult tumor to treat with very poor prognosis. **Aim** - To compare the response to teletherapy treatment (external beam radiotherapy) alone versus teletherapy combined with brachytherapy for patients with advanced squamous cell carcinoma of the esophagus. **Methods** - Were studied 49 patients with advanced squamous cell carcinoma of the esophagus on clinical stage III (TNM-1999). They were separated into two groups. The first, underwent radiation therapy alone with linear accelerator of particles, average dose of 6000 cGy and the second to external beam radiation therapy at a dose of 5040 cGy combined with brachytherapy with Iridium 192 at a dose of 1500 cGy. Brachytherapy started one to two weeks after the end of teletherapy, and it was divided into three weekly applications of 500 cGy. Age, gender, race, habits (smoking and drinking), body mass index (BMI), complications with treatment benefits (pain relief and food satisfaction) and survival were analyzed. **Results** - The quality of life (food satisfaction, and pain palliation of dysphagia) were better in the group treated with external beam radiation therapy combined with brachytherapy. Survival was higher in the brachytherapy combined with external beam radiation therapy alone. **Conclusion** - Although the cure rate of squamous cell cancer of the esophagus is almost nil when treated with irradiation alone, this therapy is a form of palliative treatment for most patients in whom surgical contraindication exists.

HEADINGS - Esophageal neoplasm. Esophagus. Radiotherapy. Brachytherapy.

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DESCRITORES - Neoplasias esofágicas. Esôfago. Radioterapia. Braquiterapia.

RESUMO - Racional - O câncer do esôfago ainda constitui neoplasia de difícil tratamento e de prognóstico muito ruim. **Objetivo** - Comparar a resposta do tratamento exclusivo com teleterapia isolada versus teleterapia associada à braquiterapia endoluminal de doentes portadores de carcinoma espinocelular avançado do esôfago. **Método** - Foram estudados 49 doentes portadores de carcinoma espinocelular avançado do esôfago médio em estágio clínico III (TNM). Os doentes foram divididos em dois grupos de doentes. O primeiro grupo foi submetido à teleterapia exclusiva com acelerador linear de partículas, dose média de 6000 cGy e o segundo à teleterapia na dose de 5040 cGy associada à braquiterapia endoluminal com Iridium 192 na dose de 1500 cGy. A braquiterapia foi iniciada uma a duas semanas após o término da teleterapia e dividida em três aplicações semanais de 500 cGy. Foram avaliadas as variáveis idade, sexo, raça, hábitos (tabagismo e etilismo), índice de massa corpórea (IMC), complicações com o tratamento, benefícios (melhora da dor e satisfação alimentar) e sobrevivência. **Resultados** - Os resultados quanto a qualidade de vida (satisfação alimentar, palição da disfagia e dor) foram melhores no grupo submetido à teleterapia associada a braquiterapia. A sobrevivência foi maior no grupo de teleterapia associada a braquiterapia. **Conclusão** - Apesar do índice de cura do câncer espinocelular do esôfago ser quase nulo quando tratado com irradiação isolada, esta terapêutica constitui-se em uma forma de tratamento paliativo para grande parte dos doentes em que existe contra-indicação cirúrgica.

INTRODUCTION

Esophageal cancer is uncommon condition, but with a poor prognosis mainly because the majority of patients already present at diagnosis with advanced disease^{1,4,15,25}. In the West 80% of patients are diagnosed when the tumor is greater than 5 cm and / or with involvement of extraesophageal mediastinal structures. Surgery is the only way for radical treatment and, consequently, improved survival, but due to the advanced stage of these patients, palliation is the treatment option most often used²¹.

Palliative treatment is important in cancer of the esophagus, as dysphagia, odynophagia, drooling, coughing and weight loss among other symptoms are limiting and cause very bad quality of life²⁹. Among the various types of non-surgical palliative treatment stands out radiation therapy (teletherapy) with satisfactory results with low morbidity and mortality^{5,10,19,22,24}.

The technique of radiation therapy alone is limited by external radiation tolerance of adjacent esophageal tissues^{8,17,18}. Brachytherapy allows a higher concentration of radiation directly into the lesion. It provides significantly lower doses to surrounding normal tissues, which allows lower dose, less morbidity and fewer side effects^{9,12}.

Looking for palliative care that provides lower morbimortality and better quality of life, the authors proposed to compare groups of patients with advanced squamous cell carcinoma of the esophagus by two methods ie, with radiation therapy alone versus teletherapy associated to brachytherapy.

METHODS

Retrospective study conducted at the Cancer Institute Arnaldo Vieira de Carvalho, from 1998 to 2004. In the same period were seen at this institution 129 patients with squamous cell carcinoma of the esophagus, of which 117 patients were located in the middle esophagus.

The patients included were considered inoperable, due to local advanced disease, decompensated comorbidities (diabetes mellitus, heart disease and lung disease) or patients who did not agree with surgical treatment, when exposed to its risks.

The variables evaluated were age, sex, race, smoking, alcohol consumption, body mass index (BMI), complications with treatment benefits with treatment and survival. Before treatment all patients underwent clinical staging with ancillary esophagogastroduodenoscopy, abdominal ultrasound, computed tomography of the thorax and

abdomen, contrast radiography of the esophagus, bronchoscopy, bone scintigraphy, and biochemical blood tests (including liver function tests). This study was approved by the ethics committee of the institution. The clinical stage was divided into stage III (57 patients), stage IV (49 patients) and I / II (11 patients) according to the TNM-1998.

Patients stage III and IV were divided into two groups with 27 patients in Group I and Group II with 22 patients.

Group I

Patients underwent teletherapy treatment alone at a dose of 6000 cGy in Varian ® linear accelerator, with 16 MV focus/skin of 80 cm. The irradiation period was 25 days at a dose of 240 cGy / day.

Group II

Patients underwent external beam radiation therapy at a dose of 5.040cGy (28x180 cGy) in the same linear accelerator of 16MV and, one to two weeks, these patients underwent brachytherapy (Nucletron ® of Iridium-192). The total dose was 1500 cGy (500 cGy/week) using catheters of 6 mm or 8 mm in diameter. The dose to be held was located 1 cm from the center of the catheter with the calculation of a margin of 2 cm both proximally and distally. The margins were evaluated by esophagoscopy or contrast radiography of the esophagus.

RESULTS

Of the 27 patients in Group I only 20 completed the proposed treatment. Seven did not due esophagotraqueal fistulas (3) and four did not support the treatment. Of the 22 from Group II, 20 completed the treatment and two were excluded because they performed only one session of brachytherapy refusing the other, due the nasogastric tube.

There was no difference between groups regarding age, sex, race, body mass index and other demographic variables. The alcoholism and smoking were highly prevalent in both groups.

There was no progression of disease in any patient during treatment and no mortality. Both groups were followed every three months until death through clinical consultation, esophagoscopy, chest and abdomen CT, hematological and biochemical tests.

In cases with stenosis of the irradiated area, the patients underwent endoscopic dilatation (three cases in Group I and seven in Group II). Patients who developed tracheo or bronquialesophageal fistula (three cases in Group I) were implanted Malafaia

prosthesis.

The patient characteristics of each group are described in Table 1.

TABLE 1 – Epidemiological data of treated patients

	Group I	Group II
Age	(42-81) 60.3 a	(48-90) 65.2
Race	White: 17 Blacks : 3	White : 17 Blacks : 3
Sex	Male: 17 Female : 3	Male: 15 Female: 3
Smoking	Yes: 19 No : 1	Yes: 15 No: 6
alcoholism	Sim : 16 No : 1	Yes: 14 No: 5
Body mass index (BMI)	(12-22.2) 18,35	(16 – 24.2) 19,6
Clinical Stage (TNM)	III	III
Size	(2,5 –10cm) 5.25	(2-10cm) 5.26

Complications with the treatments

Although there was no significant difference between the two groups, was observed that Group I presented three cases of esofagotraqueal or bronchial fistulas, which was not observed in Group II, but the rate of stenosis was higher in Group II (seven cases) than in Group I (three cases) (Table 2).

TABLE 2 – Complications related to the treatments

	Teletherapy		Teletherapy + brachytherapy		Total	
	N	%	N	%	N	%
Actinic esophagitis	1	5%	0	0%	1	2,5%
Esophageal stenosis	3	15%	7	35%	10	25%
Esophagotraqueal fistula	3	15%	0	0	3	7,5%
No complication	13	65%	13	65%	26	65%
Total	20	100%	20	100%	40	100%

Chi-square (p) = 1.000 not significant

There was no difference between groups regarding the distribution of complications.

Benefits of treatment

Both groups benefited from treatment, especially with regard to the quality of food intake and pain relief, with a slight prevalence in Group II but not statistically significant (Table 3).

TABLE 3 – Clinical benefits with treatments

		GROUP					
		Teletherapy		Teletherapy + brachytherapy		Total	
		N	%	N	%	N	%
Benefits	Yes	17	85%	19	95%	36	90%
	No	3	15%	1	5%	4	10%
Total		20	100%	20	100%	40	1000%

Chi-square (p) 0598 = not significant

Survival (in days)

It can be seen in Table 4 and Figures 1 and 2, Group II had higher survival than Group I. Perhaps this fact may be related to food quality, as in Group I patients fed up with liquids and pastes (11 patients), six with normal diet after treatment and three were not fed.

TABLE 4 – Survival in days

	Teletherapy	Teletherapy+braq.
Average	276,80	557,70
Standard deviation	233,70	380,06
n	20	20
	105,1	170,9

T teste (p) = 0.008*

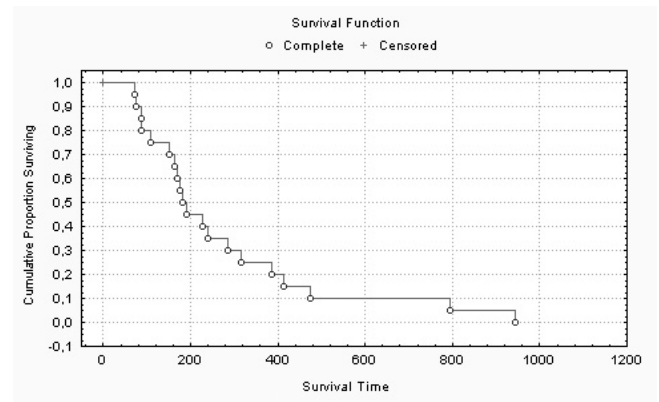


FIGURE 1 - Survival analysis for Group I (teletherapy) Kaplan-Meier

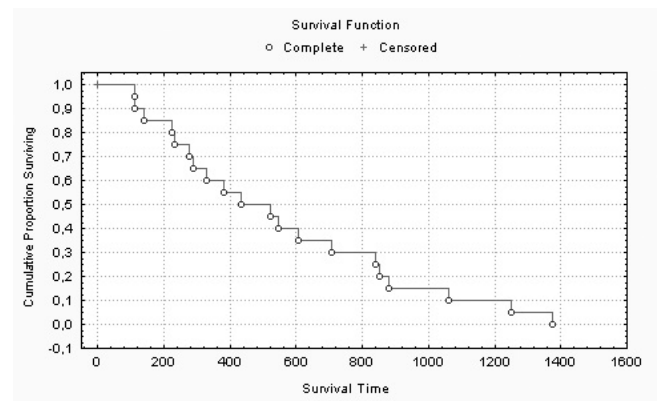


FIGURE 2 - Survival analysis for Group II (teletherapy + brachytherapy) Kaplan-Meier

In Group II, even after the dilatation, 13 patients fed with normal diet and six with liquids and pastes. One patient did not feed.

Death of patients occurred primarily due distant metastases and other medical complications not related to cancer or treatment.

DISCUSSION

Tumors of the esophagus have been described more than 2,000 years in Honan Province, northwest China. A Persian writer of medical affairs called Jurgani also described at the beginning of 1100 BC. There is great geographical variation in its incidence, with high prevalence in parts of Asia, Africa, Iran, France and South America^{1,21,25,30}. In terms of incidence are referred to 130 cases per 100,000 inhabitants per year in China, 115 cases in Iran, 29 in France and 25 in Brazil. If only the southern region of Brazil is considered the incidence reaches 44 cases per 100 000 inhabitants⁵.

Approximately 95% of esophageal cancers consist of squamous cell carcinomas and 4% to 5% are adenocarcinomas^{1,4,5,10,24,25}.

The prognostic factors are related to age, sex, smoking, alcoholism, weight loss and body mass index (BMI) but there are factors related to the tumor itself, such as location, extent and degree of tumor penetration into the wall (T), metastatic lymph nodes (N), degree of histological differentiation, presence of hematogenous and lymphatic invasion and the presence of distant metastases^{11,16,27}. The authors found a higher prevalence of males over the age of 60 years, consumption of alcohol and tobacco in patients with squamous cell carcinoma of the esophagus which is in accordance with the literature. Prevalence was higher in white people probably due to the region (state of São Paulo) where patients live. In this region the proportion of white people is higher than blacks. Smoking and alcohol are factors present in these patients with squamous cell carcinoma of the esophagus, as far as it is in the literature^{3,7,14,26}.

Although surgery is still the preferred treatment for this disease, it is only possible to be more radical in the initial stages, although with low cure and high rates of morbidity and mortality. Therefore, remains palliation surgical or not to minimize the suffering of these patients^{13,29}.

The palliative radiotherapy aims at controlling pain and esophageal permeation so the patient can be fed, preferably by solids. The oral feeding is a key factor in quality of life of these patients, since many patients have low socioeconomic status which hinders the acquisition of enteral feeding. It can be easy handling and with high calories, but are expensive and restricted to large centers.

In recent years, ostomy (gastrostomy and jejunostomy) is undertaken only as a palliative treatment in exceptional cases. This position mainly aimed at poor quality of life for patients with these stomas. Leakage problems, special diets, discomfort and inability to socialize because the patient can not eat by mouth, are the main complications.

The endoluminal brachytherapy became more widespread and achieve further development after the advent of the high-dose rate²⁷. The prescription should follow the regimen used in teletherapy, dose/fraction, number of fractions, interval between fractions and total dose. The specification of the dose should be standardized and reproducible²⁰.

Pearson et al. published in 1969 encouraging results of 20% survival at five years with teletherapy alone in squamous cell cancer of the esophagus. Newaisky et al. in 1982, updated the results of Pearson, checking survival of 9%. Note that in most studies the five-year survival is less than 10%. No other author ever reproduce the results of Pearson^{6,23}.

The teletherapy alone led to three tracheoesophageal fistula, while the association of teletherapy and brachytherapy showed no leaks. Although the association showed a larger number of esophageal stenosis, they were overcome by endoscopic dilatation, providing nutrition closer to normal, than external beam radiation therapy alone².

The association had higher survival rate suggesting that the method provides a better locoregional control.

There was no interference in the outcome on other studied items (age, gender, race, smoking, alcohol consumption, and body mass index), since there was no significant difference between groups.

CONCLUSION

Although the cure rate of squamous cell cancer of the esophagus is almost nil when treated with irradiation alone, this therapy is in a form of palliative treatment for most patients in whom surgical contraindication exists.

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