Profile of Patients with Esophageal Cancer Diagnosed Between 2001 and 2010 in Brazil

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Perfil dos Pacientes com Câncer de Esôfago Diagnosticados entre 2001 e 2010 no Brasil

Perfil de los Pacientes con Cáncer de Esófago Diagnosticados entre 2001 y 2010 en Brasil

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Abstract

Introduction: Esophageal cancer is the third most common neoplasm of the digestive tract and presents poor prognosis when diagnosed in advanced stages of the disease. **Objective:** To describe the socio-demographic, clinical and treatment characteristics of patients diagnosed with esophageal cancer in Brazil, from 2001 to 2010. **Method:** A cross-sectional study of patients with esophageal cancer registered between 2001 and 2010 in Hospital-based registries. Socio-demographic, clinical and treatment variables were analyzed. Descriptive analysis was performed using mean and standard deviation for continuous variables, and absolute and relative frequency for categorical variables. **Results:** A total of 24,204 patients were included, with a mean age of 60.8 years (± 11.5). The majority of the population was male (78.3%), with a low level of schooling (75.2%), alcoholics (62.9%), smokers (76.0%), and had an advanced stage of diagnosis (41.3% in clinical stage III and 26.9% in stage IV), the topographic group being the most prevalent was in the esophagus upper and middle (76.4%). 12.7% of the patients were not submitted to any cancer treatment. The most frequent treatments were the combination of radiotherapy and chemotherapy (25.6%), and treatment alone with radiotherapy (21.9%). At the end of the first cancer treatment, 10.7% had no evidence of disease, 8.4% had partial remission, 26.6% had a stable disease, and the remaining patients had progression or death (54.4%). **Conclusion:** In Brazil, the cases diagnosed for esophageal cancer are mostly diagnosed in advanced stages of the disease, which represents greater therapeutic aggressiveness and worse response to treatment.

Key words: Esophageal Neoplasms; Risk Factors; Neoplasm Staging; Brazil; Electronic Health Records.

Resumo

Introdução: O câncer de esôfago é a terceira neoplasia mais comum do trato digestivo e apresenta prognóstico ruim quando diagnosticado em estádios avançados da doença. **Objetivo:** Descrever as características sociodemográficas, clínicas e de tratamento dos pacientes diagnosticados com câncer de esôfago no Brasil, no período de 2001 a 2010. **Método:** Estudo transversal de base secundária em pacientes com câncer de esôfago, cadastrados entre 2001 e 2010, nos Registros Hospitalares de Câncer. Foram analisadas as variáveis sociodemográficas, clínicas e de tratamento. Foi realizada análise descritiva utilizando média e desvio-padrão para as variáveis contínuas, e frequência absoluta e relativa para as categóricas. **Resultados**: Foram incluídos 24.204 pacientes, com média de idade de 60,8 anos (±11,5). A maioria da população era do sexo masculino (78,3%), de baixa escolaridade (75,2%), etilista (62,9%), tabagista (76,0%) e com estádio avançado ao diagnóstico (41,3% em estádio clínico III e 26,9%, IV), sendo o grupo topográfico de maior prevalência o esôfago superior e médio (76,4%). Não foram submetidos a nenhum tratamento oncológico 12,7% dos pacientes. Os tratamentos mais frequentes foram a combinação entre radioterapia e quimioterapia (25,6%) e o tratamento isolado com radioterapia (21,9%). Ao final do primeiro tratamento oncológico, 10,7% estavam sem evidência de doença, 8,4% com remissão parcial, 26,6% com doença estável e, os demais, com doença em progressão ou óbito (54,4%). C**onclusão**: No Brasil, os casos diagnosticados por câncer de esôfago são, em sua maioria, diagnosticados em estádios avançados da doença, o que representou maior agressividade terapêutica e pior resposta ao tratamento.

Palavras-chave: Neoplasias Esofágicas; Fatores de Risco; Estadiamento de Neoplasias; Brasil; Registros Eletrônicos de Saúde.

Resumen

Introducción: El cáncer de esófago es la tercera neoplasia más común del tracto digestivo y presenta un pronóstico malo cuando se diagnostica en estadios avanzados de la enfermedad. **Objetivo:** Describir las características sociodemográficas, clínicas y de tratamiento de los pacientes diagnosticados con cáncer de esófago en Brasil, en el período de 2001 a 2010. **Método:** Estudio transversal de base secundaria en pacientes con cáncer de esófago, registrados entre 2001 y 2010, en los Registros Hospitalarios de Cáncer. Se analizaron las variables sociodemográficas, clínicas y de tratamiento. Se realizó un análisis descriptivo utilizando media y desviación estándar, para las variables continuas, y frecuencia absoluta y relativa para las categóricas. **Resultados:** Se incluyeron 24.204 pacientes, con una media de edad de 60,8 años (±11,5). La mayoría de la población era del sexo masculino (78,3%), de baja escolaridade (75,2%), etilista (62,9%), tabaquista (76,0%) y con estadio avanzado al diagnóstico (41,3% en estadio clínico III y 26,9% en estadio IV), siendo el grupo topográfico de mayor prevalencia el esófago superior y medio (76,4%). No fueron sometidos a ningún tratamiento oncológico, el 12,7% de los pacientes. Los tratamientos más frecuentes fueron la combinación entre radioterapia y quimioterapia (25,6%), y el tratamiento aislado con radioterapia (21,9%). Al final del primer tratamiento oncológico, el 10,7% estaba sin evidencia de enfermedad, el 8,4% con remisión parcial, el 26,6% con enfermedad estable y los demás, con enfermedad en progresión o muerte (54,4%). **Conclusión:** En Brasil, los casos diagnosticados por cáncer de esófago son en su mayoría, diagnosticados en estadios avanzados de la enfermedad, lo que representó mayor agresividad terapéutica y peor respuesta al tratamiento.

Palabras clave: Neoplasias Esofágicas; Factores de Riesgo; Estadificación de Neoplasias; Brasil; Registros Electrónicos de Salud.

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INTRODUCTION

Esophageal cancer is the third most common neoplasm of the digestive tract. Currently is the seventh type of cancer most frequent in the whole world and the sixth cause more common of death by cancer in 2018. The distribution of this type of neoplasm is well heterogeneous in the world, being more common in less developed areas[1]. In Brazil, 2018, 8,240 esophageal cancer cases are estimated in men and 2,550 in women[2].

The most frequent histological type is the squamous cell carcinoma (SCC); but international studies show the gradual reduction of this type of tumor and the elevation of the frequency of adenocarcinoma[3-7].

The etiology of the esophageal cancer is related to the interaction with several risk factors, like : age, family background, tobacco, alcoholism, oral fungal infections, excessive use of vitamin A, fungal toxins and intake of high temperature mate. Affections like megaesophagus, caustic esophageal stenosis and Barrett esophagus also contribute significantly for its development. Therefore, lifestyle associated to nutrition habits is a key factor for the genesis of malignant esophageal tumors. [5].

Esophageal cancer is a disease with poor prognosis[4,8], and only a reduced group of patients is eligible to treatment with curative intent[9-10]. Strategies using radiotherapy and combination of radiotherapy with chemotherapy to extend the survival and minimize the complications of the treatment have called the attention of the scientific community [10-11]. However, despite the progress of esophageal cancer treatment in the last years, the survival of the patients, even after complete resection, continues quite low because of the advanced stage in the diagnosis[3-4,12-14].This happens, mainly, because the signs of cancer occur only when the tumor reaches a significant volume to provoke obstructive symptoms. With the progression of the obstruction, pain and excessive salivation occur regularly, in addition to weight loss, bleeding, chest pain and vomits[15-16].

Another probable factor associated to the worsening of the prognosis is the interval between the onset of the symptoms and the diagnosis. In a study performed in Mexican hospitals, the time between the onset of the symptoms and the diagnosis varied between seven and 25 months and 90.5% of the cases were diagnosed later[17].

The late diagnosis of esophageal cancer increases its lethality. Studies describing the clinical and demographic aspects may help to implement preventive measures through education of the population, early detection of the tumor and care supplied to patients diagnosed with this neoplasm.

In this context, this study has the objective to describe the social-demographic, clinical and treatment characteristics of the patients diagnosed with esophageal cancer registered in cancer hospitals records in Brazil from 2001 to 2010.

METHOD

It is a secondary base cross-sectional study using the data of Cancer Hospital Records of the State of São Paulo coordinated by "Fundação Oncocentro de São Paulo (Fosp)" and of the "Módulo Integrador do Registros Hospitalares de Câncer" (Integrating Module of Cancer Hospital Records) offered by "Instituto Nacional de Câncer José Alencar Gomes da Silva (INCA)" .

All the cases registered with esophageal cancer diagnosis were included based in the 10th. Revision of the International Classification of Health Related Problems and Diseases, (CID 10)18, C15.0 until C15 from 2001 to 2010 submitted to management and treatment in the same hospital unit. The cases under 18 years old and older than 100 years, unknown gender, esophageal non-primary or unknown histological types were excluded.

The following variables were analyzed: age (continuous), age group (categorized in subgroups every 5 years), race (Caucasian, black, Asian, brown, Indian), classified as Caucasian and others, education level (illiterate, 1 to 7 years of education, 8 to 12 years of education and more than 12 years of education ,later grouped in low (up to 8 years of education) and high education level (> 8 years), marital status (with spouse, married and without spouse), widows, divorced and single women, smoking and alcoholism (categorized in never, ex and yes), area of the residence (capital and rural), year of the diagnosis in quinquennial (2001-2005 and 2006-2010), histological type according to the 3rd. edition of the International Classification of Diseases for Oncology (ICD-0) of the World Health Organization - WHO19,categorized in adenocarcinoma (morphological codes 8140-8575), SCC (8050-8084) and other histological types (8003-8041); the topographies were classified as: medium and upper esophageal (C15.0, C15.3, C15.4; for the codes C15.8 and C15.9, it were included only the histologies 8050-8083), lower esophageal (C15.2, C15.5; for codes C15.8 and C15.9, it were included only the histologies 8140-8576), other non-specified areas of the esophageal (C15.8, C15.9) excluding the histologies 8050-8083 and 8140-8576); clinical staging according to the Tumor, Node and Metastasis (TNM)20 – staging from 0 to IV –; treatment performed; response in the end of the first trimester classified in: absence of evidence of the disease in the end of the treatment, partial remission, stable disease or in progression, therapeutic support and death; time passed between the diagnosis and the beginning of

the treatment (in days), being excluded of the analyzes the negative times (when the beginning of the treatment happened earlier than the date of the diagnosis) and those with time period over one year (because of the possibility of errors in the registry of the dates).

It was utilized the statistic software *Statistical Package for the Social Sciences* (SPSS) version 23.0, for data analysis with a descriptive analysis of the population, determining the frequency of the categorical variables analyzed. It was calculated the mean and respective standard deviation for the variables age and time between the diagnosis and beginning of the treatment. INCA Institutional Review Board approved this study, number 128/11.

RESULTS

It were included 24,204 patients diagnosed with esophageal cancer between 2001 and 2010, drawn from registries of 239 hospital facilities located across all the Brazilian regions. Considering the period studied, the mean age of the population at the diagnosis was 60.8 years (± 11.5), the age group of 55 to 59 years was the most prevalent age group (Figure 1).

The descriptive analysis of the social-demographic variables is presented in Table 1. The majority of the population were males (78.3%), declared of Caucasian race (47.5%), illiterate or incomplete elementary school (75.2%), alcoholic (62.9%), tobacco users (76.0%) and married (58.1%). As for the region of domicile, 83.4% were from the Southern and Southeast regions.

For hospital units, 63.5% were located in Brazil Southeast Region. The majority of the patients (87.6%) were enrolled at SUS (National Health System) and registered at the unit of high complexity with diagnosis and no previous oncologic treatment (71.3%). The diagnosis of cancer was advanced, 41.3% in clinical staging III and 26.9%, staging IV. Concerning the tumoral aspects, the topographic group with major prevalence was medium and upper esophageal (76.4%) and histological type SCC (82.4%) (Table 2).

No oncological treatment was provided to 12.7% of the patients. Among those who were treated, the average time passed between the diagnosis and the treatment was 62 days (±52) and in 58.0% of the cases, the treatment was implemented in until 60 days after the diagnosis. The most frequent treatments were the combination of radiotherapy and chemotherapy (25.6%), radiotherapy isolated treatment (21.9%) and surgery (13.6%). In the end of the first trimester of oncological treatment, 10.7% showed no evidence of the disease, 8.4% with partial remission, 26.6% with stable disease and the others (54.4%) with disease in progression or death (Table 3).

DISCUSSION

This study describes the social-demographic, clinical profile and treatment of the patients diagnosed with esophageal cancer in Brazil from 2000 to 2010. The majority of the population was from Brazil's Southeast Region, males, low education level, diagnosis of SCC located in the medium and upper esophageal in advanced stages of the disease.

The demographic characteristics encountered in our study concur with results published for other populations where black men presented major frequency of esophageal cancer, older than 60 years and low education level [6-9,17-23]. Also, the use of tobacco and alcohol is more frequent in this population, which can explain the occurrence of cancer in persons with these characteristics [5,21].

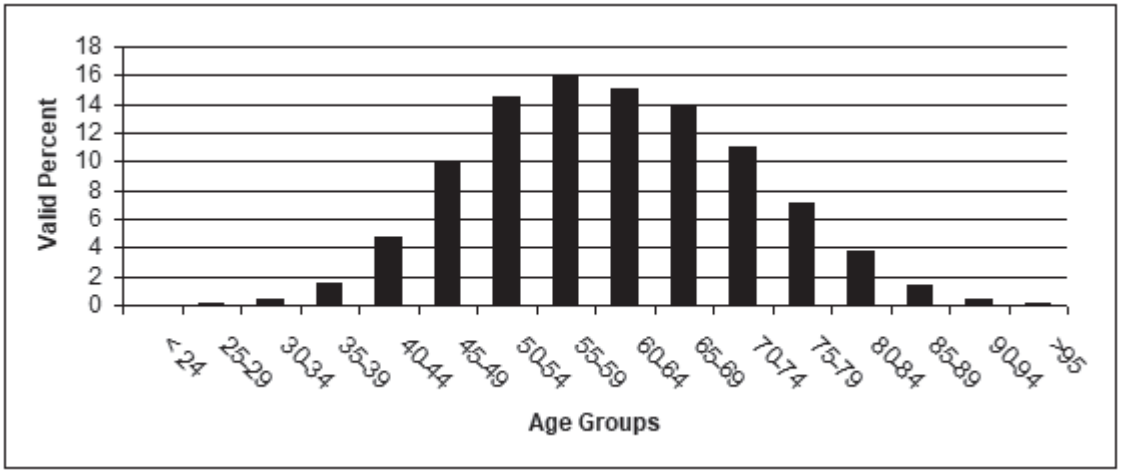

Figure 1. Percent distribution of age group of the cases of esophageal cancer, Brazil, 2001 to 2010 (n=24,204)

Table 1. Descriptive analysis of the social-demographic characteristics of the cases of esophageal cancer, Brazil, 2001 to 2010 (n=24,204)

Variable	N	% Total	% Valid
Gender			
Male	18.960	78,3	78,3
Female	5.244	21,7	21,7
Race reported			
Caucasian	6.778	28,0	47,5
Brown	5.636	23,2	39,5
Black	1.716	7,1	12,0
Asian	134	0,6	0,9
Indian	19	0,1	0,1
Unknown	9.921	41,0	---
Education Level			
Illiterate	3.658	15,1	21,7
Incomplete elementary school	9.046	37,4	53,5
Complete elementary school	2.856	11,8	16,9
High school	1.020	4,2	6,0
College	313	1,3	1,9
Unknown	7.311	30,2	---
Cancer Family Background			
Yes	2.662	11,0	35,1
No	4.922	20,3	64,9
Unknown	16.620	68,7	---
Alcohol use at the diagnosis			
Never	3.660	15,2	34,2
Ex-user	317	1,3	3,0
Yes	6.737	27,8	62,8
Unknown	13.490	55,7	---
Tobacco user at the diagnosis			
Never	2.429	10,0	21,4
Ex-user	292	1,2	2,6
Yes	8.611	35,6	76,0
Unknown	12.872	53,2	---
Marital State			
Single	2.960	12,3	21,0
Married	8.172	33,8	58,1
Widower	2.039	8,4	14,5
Judicially separated	905	3,7	6,4
Unknown	10.128	41,8	---
Region of residence			
North	373	1,5	1,5
Northeast	3.060	12,6	12,6
West-Central	567	2,3	2,3
Southeast	15.348	63,5	63,6
South	4.805	19,9	20,0
Unknown	51	0,2	---
Place of residence			
Capital	2.585	10,7	10,7
Rural	21.569	89,1	89,3
Unknown	50	0,2	---

Table 2. Descriptive analysis of the characteristics at the diagnosis of the esophageal cancer cases, Brazil, 2001 to 2010 (n=24,204)

Variable	N	% Total	% Valid
Region of the hospital facility			
North	311	1,3	1,3
Northeast	3.007	12,4	12,4
West-Central	439	1,8	1,8
Southeast	15.621	64,6	64,6
South	4.826	19,9	19,9
Origin of the referral			
SUS	12.237	50,5	87,6
Non SUS	1.489	6,2	10,6
Self decision	246	1,0	1,8
Unknown	10.232	42,3	---
Register at the hospital facility			
Without diagnosis and without treatment	6.951	28,7	28,7
With diagnosis and without treatment	17.253	71,3	71,3
Staging			
0	90	0,4	0,6
I	526	2,2	3,4
II	4.275	17,6	27,8
III	6.363	26,3	41,3
IV	4.151	17,2	26,9
Unkonw	8.799	36,3	---
Topographic Group			
Medium and upper esophageal	18.496	76,4	76,4
Lower esophageal	4.515	18,7	18,7
Other esophageal non-specified areas	1.191	4,9	4,9
Unknown	02	0,0	---
Histological type			
Adenocarcinoma (8140-8575)	2.306	9,5	9,5
Squamous cell carcinoma of squamous cells (8050-8084)	19.955	82,5	82,5
Other types (8003-8041)	1.943	8,0	8,0

The majority of the population in this study reported the consumption of alcohol and tobacco at the moment it was made the diagnosis of esophageal cancer. These habits are known as important risk factors and prognosis of esophageal cancer and in different populations[7,23-24]. In another study, 72% of the individuals with esophageal cancer were tobacco users and 68% consumed alcoholic beverages. In general, the risk of esophageal cancer among tobacco users is two-fold to five time higher when compared to non-tobacco users, while for chain-tobacco users, the risk can reach 10 times[9]. A systematic revision observed the raise of esophageal cancer type SCC because

Table 3. Descriptive analysis of the characteristics of the esophageal cancer cases treatment, Brazil, 2001 to 2010 (n=24,204)

Variable	N	% Total	% Valid
Time between the diagnosis and beginning of the treatment (n=21,004)*			
0 to 29 days	6,223	25.7	30.0
30 to 59 days	5,799	24.0	28.0
60 to 89 days	3,957	16.3	19.1
90 a 119 days	2,200	9.1	10.7
≥ 120 days	2,530	10.5	12.2
Unknown	3,495	14.4	---
Treatments performed			
No treatment	3,053	12.6	12.7
Surgery	3,278	13.5	13.6
Radiotherapy	5,266	21.8	21.9
Chemotherapy	3,155	13.0	13.1
Surgery and radiotherapy	715	3.0	3.0
Surgery and chemotherapy	550	2.3	2.3
Radiotherapy and chemotherapy	6,150	25.4	25.6
Surgery. chemotherapy and radiotherapy	966	4.0	4.0
Other combinations and treatments	924	3.8	3.8
Unknown	147	0.6	---
Response in the end of the first treatment (n=21,004)*			
No evidence of the disease	1,730	7.1	10.7
Partial remission	1,365	5.6	8.4
Stable disease	4,306	17.8	26.6
Disease in progression	2,399	9.9	14.8
Therapeutic support	322	1.3	2.0
Death	6,053	25.0	37.5
Unknown	8,029	33.3	---

* Considering only those submitted to oncologic treatment

of alcohol use with dose-response effect, i.e, the higher daily intake, higher the risk of developing this type of cancer (varying from 1.32 for the use of 1 to 2 daily doses until 4.12 for the use of higher than ten daily doses)[25]. In a study using cancer hospital records in Brazil, after adjustment, it was identified a fraction assigned to tobacco of 58.9% in esophageal cancer development[26] and 46.9% to alcohol use[27].

In this study, 91.6% of the esophageal cancer cases were SCC, a predominant histological type in the world[3,7,12,23] and in Brazil[15]. Nonetheless, several studies are showing a drop of SCC cases and rise of adenocarcinoma cases[3-7], which likely occurs because of the increase of risk factors exposure as obesity, overweight associated to gastric juice reflux, use of tobacco and alcohol[28].

Esophageal cancer is insidious and its symptoms usually occur in the most advanced phases of the disease; the most frequent symptoms are dysphagia, retrosternal pain and odynophagia [15]. The lack of symptoms in early phases, in the majority of cases, pushes the diagnosis to more advanced phases [16], which makes this cancer highly lethal[18]. In this study, 68.2% of the patients diagnosed in advanced stages, which was similar to what was encountered in other populations, which implied in more aggressive treatment, higher frequency of oncologic therapy-related complications and worse prognosis[3-4,9,12-13].

Among those who were treated, the most frequent regimens were the combination of radiotherapy and chemotherapy and the isolated use of radiotherapy as addressed in this study. In the end of the first oncologic treatment, 37.4% died, 26.6% stabilized and for 14.8% the disease was in progression. In another study, the patients submitted to radiotherapy for esophageal cancer treatment were younger, with advanced disease, histological type SCC and were not submitted to surgery. Further, this group presented higher risk of death per cardiopathy in comparison to those submitted to other treatments (HR=1.96 IC 95% 1.47-2.64)[11].

Because this study used secondary data, the main limitation is the lack of important demographic, clinical and prognosis information. Some variables listed in the form of data collection of cancer hospital records continue as non-mandatory, which may have caused the lack of information observed. However, it presents the profile of the diagnosed patients and treated for esophageal cancer in SUS-approved hospital facilities in Brazil along an extended time period. These information can be useful for the planning of healthcare actions and to demonstrate the importance of using data drawn from cancer hospital records.

CONCLUSION

In Brazil, the profile of esophageal cancer diagnosed cases is, in its majority, in males, with low education level, tobacco users and alcoholic. They were diagnosed in advanced stages of the disease, which implied in more aggressive treatment and worse therapeutic response. Though the beginning of the treatment had occurred in less than 60 days for most part of the esophageal cancer cases diagnosed in Brazil between 2001 and 2010 (58.0%), it was noticed a high percent with lack of therapeutic response to the first treatment (54.4%); this can be attributed to late diagnosis (68.2% of the cases were diagnosed in stages III or IV), limiting the therapeutic options and, consequently, negatively impacting the prognosis of these patients. In this scenario, the public

policies should focus in educational strategies to promote every type of prevention and control of esophageal cancer in Brazil.

CONTRIBUTIONS

Ariane Igreja Buccos Marinho Cruz contributed substantially for the study design, data analysis and wording and approval of the published version. Luis Felipe Ribeiro Pinto contributed substantially for the study design, data interpretation as well as for the critical revision and final approval of the published version. Luiz Claudio Santos Thuler contributed substantially for the study design, data interpretation as well as for the critical revision and final approval of the published version. Anke Bergmann contributed substantially for the study design, data interpretation as well as for the wording and final approval of the published version.

DECLARATION OF CONFLICT OF INTERESTS

The author Anke Bergmann states potential conflict of interests because she is scientific editor of "Revista Brasileira de Cancerologia" of INCA. The other authors have no conflict of interest.

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