Epidemiological features of esophageal cancer. Squamous cell carcinoma versus adenocarcinoma[1]

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ABSTRACT

PURPOSE: To analyze the epidemiological features of patients with esophageal cancer according to the histopathological types: squamous cell carcinoma or adenocarcinoma.

METHODS: A total of 100 patients with esophageal cancer, being 50 squamous cell carcinomas and 50 adenocarcinomas were analyzed for demographics, nutritional factors, lifestyle habits, benign pathological conditions associated, like Barrett's esophagus and megaesophagus, tumor stage and survival rates. The nutritional factors evaluated included body mass index, percent weight loss, hemoglobin and albumin serum levels.

RESULTS: Esophageal cancer occurred more often in men over 50 years-old in both histological groups. No significant differences on age and gender were found between the histological groups. Squamous cell carcinoma was significantly more frequent in blacks than adenocarcinoma. Alcohol consumption and smoking were significantly associated with squamous cell carcinoma. Higher values of body mass index were seen in patients with adenocarcinoma. Barrett's esophagus was found in nine patients (18%) with adenocarcinoma, and megaesophagus in two patients (4%) with squamous cell carcinoma. The majority of patients were on stages III and IV in both histological groups. The mean survival rates were 7.7 ± 9.5 months for patients with squamous cell carcinoma and 8.0 ± 10.9 months for patients with adenocarcinoma. No significant differences on tumor stage and survival rates were detected between the histological groups.

CONCLUSION: Epidemiological features are distinct for the histopathological types of esophageal cancer. Squamous cell carcinoma is associated with black race, alcohol and smoking, while adenocarcinoma is related to higher body mass index, white race and Barrett's esophagus.

Key words: Esophageal Neoplasms. Carcinoma, Squamous Cell. Adenocarcinoma. Epidemiology.

Introduction

Esophageal cancer (EC) is one of the most aggressive neoplasms that affect the gastrointestinal tract as a result of its late diagnosis, older age and nutritional disorders due to esophageal obstruction and the impossibility of proper food ingestion[1,2].

Another characteristic of EC is its incidence diversity, with high indices in Asian countries[3,4] and a milder incidence in European and American continents. A great diversity is also observed in Brazil, with four cases in every 100 thousand inhabitants in the North Region and 15 cases for the same size population in South Brazil[2].

Esophageal cancer is more frequent in older male individuals[5,6], generally being associated with ethylism and tabagism[7], intake of hot drinks and foods[8], vitamin deficiencies[7], ingestion of caustic substances[9], Barrett Esophagus (BE)[10], megaesophagus[11] and human papiloma virus infection[12].

Esophageal cancer is histologically classified as squamous cell carcinoma (SCC) or adenocarcinoma (ADC). SCC results from the formation of non-keratinized stratified squamous epithelium and is more common in developing countries. The preferential sites of SCC are the middle and upper thirds of the esophagus[1,13,14].

Adenocarcinoma occurs in the lower third of the esophagus and results from intestinal metaplasia (BE), due to chronic gastric reflux[10,15].

Rare histological types may also affect the esophagus, such as small cell and basaloid squamous carcinoma[16,17].

The epidemiological pattern of EC has changed in the last decades, with a significant increase in ADC over SCC[18-21]. It is worth noting that in the same period, there was also a significant increase in the incidence of obesity, which is considered a contemporary epidemic.

Considering that obesity is a risk factor for many types of cancer like breast, colon, bladder and prostate, it may also be related to a greater incidence of ADC[22-24].

The aim of the present study was to analyze possible EC (SCC and ADC) risk factors with emphasis on nutritional condition, ethylism, tabagism, and benign esophageal disorders.

Methods

This was a retrospective and comparative study of medical records of 100 EC patients referred to the Botucatu University Hospital – UNESP (BUH) from January 2007 to December 2012.

The patients were assigned to either of two groups of 50 patients according to their esophageal cancer histological type: Group 1: (n = 50) squamous cell carcinoma and Group 2: (n = 50) adenocarcinoma.

The analysis of the patients' medical records allowed the evaluation of the following parameters:

1. Demographics: age, sex, race.
2. Nutritional condition:
   Body Mass Index (BMI, kg/ m^2), calculated from the weight and height using Cronk & Roche's[2,5] formula (1982): BMI = weight divided by the squared height in meters. The collected data were compared to reference values[26].
   Percent weight loss (%WL) was calculated from the usual body weight reported by the patient and the actual body weight using the formula: %WL = (usual body weight – actual body weight x 100) divided by the actual body weight. A weight loss over 10% is considered severe according to the criteria proposed by Blackburn *et al.*[27].
   Hematimetric Evaluation: Patient and reference hemoglobin values (11.0 – 18.0 g/dL) from the BUH Hematology Laboratory were compared and found to be acceptable.
   Biochemical Evaluation: Serum albumin levels were determined by the automatic enzymatic colorimetric method in the Biochemistry Laboratory of the BUH, Clinical Analysis Sector. The obtained values were compared to the reference data[28].
3. Lifestyle: The self-report and length of ingestion of distilled drinks and tobacco smoking were assessed.
4. Benign esophageal disorders: History of megaesophagus and BE were assessed.
5. Clinical Tumor Staging was performed based on tomographic exams of the thorax and abdomen (TNM/ UICC classification – National Cancer Institute, 2012).
6. Survival rate was evaluated considering the time between endoscopic diagnosis and patient death or last interview.

Statistical analysis

The variables nutritional condition, ethylism, tabagism and survival rate were submitted to the Student t-test for independent populations. Tumor staging, sex and race results were tested with chi-square.

Results

Demographics

Table 1 gives the gender results, where it was observed a high incidence of esophageal cancer in male individuals. This result was observed in patients with SCC and ADC, without difference.

TABLE 1 – Frequency distribution for gender in SCC (Group 1) and ADC (Group 2) patients.

Group	Gender		
	Male	Female	Total
SSC	48 (96%)	2 (4%)	50
ADC	43 (86%)	7 (14%)	50
TOTAL	91 (91%)	9 (9%)	100

p = 0.08

Table 2 gives the results for age (years) of patients in groups SCC and ADC; no difference was observed between the groups. Most part of patients in two groups were over 50 years old.

TABLE 2 – Age (years) of SCC and ADC patients.

Age	Group	
	SCC	ADC
The youngest	43	34
The oldest	97	90
Mean	60.3 ± 10.6	62 ± 11.5

p = 0.31

Table 3 gives the frequency distribution for patients' race; there was a significant difference between the groups. The patients with SCC were more frequent in black individuals.

TABLE 3 – Frequency distribution for patients' race per group.

Group	Race		
	White	Black	Total
SCC	37 (74%)	13 (26%)	50
ADC	48 (96%)	02 (4%)	50
Total	85 (85%)	15 (15%)	100

p = 0.002

Nutritional condition

Table 4 gives the nutritional condition results. The highest BMI values were found in patients with ADC (significant difference).

TABLE 4 – Mean and standard deviation for nutritional condition-related variables.

	Group		
Variable	SCC	ADC	p value
BMI	18.8 ± 3.5	21.4 ± 5.8	0.007
%WL	20.0 ± 9.3	17.2 ± 8.6	0.13
Hb	13 ± 1.9	12.7 ± 2.5	0.54
SA	4.1 ± 3.6	4.5 ± 0.7	0.40

BMI = Body mass index
%WL = percent weight loss
Hb = hemoglobin
SA = Serum albumin

Lifestyle

Tables 5 and 6 present the results for length of ethylism and tabagism in SCC and ADC patients; a significant difference was observed between the two groups. The duration of ethylism and tabagism was longer in patients with SCC.

TABLE 5 – Mean and standard deviation for ethylism and tabagism length (years).

Variable	Group		
	SCC	ADC	p value
Ethylism	35.4 ± 13.7	13.7 ± 16.0	< 0.001
Tabagism	36.7 ± 14.9	25.5 ± 18.6	< 0.001

TABLE 6 – Ethylism and tabagism in SCC and ADC patients.

Habits	ESCC	EADC
Ethylism and Tabagism	45 (98%)	27 (54%)
Ethylism	02 (4%)	01 (2%)
Tabagism	02 (4%)	11 (22%)
Abstemiousness	01 (2%)	11 (22%)
Total	50 (100%)	50 (100%)

p = 0.006

Benign esophageal disorders

Table 7 gives the benign esophageal disorder frequency in SCC and ADC patients. BE was observed only in patients with ADC, and megaesophagus only in patients with SCC.

TABLE 7 – Benign esophagus disorders associated to esophageal cancer.

Disorder	SCC	ADC
Megaesophagus	02 (4%)	0
Barrett's esophagus	0	09 (18%)
Total	02	09

Cancer staging

Table 8 gives the cancer staging frequency; there was no significant difference between the groups. The most part of patients of both groups was in advanced disease.

TABLE 8 – Cancer staging frequency distribution for patients per group.

Group	Staging			
	II	III	IV	Total
SCC	1 (2%)	11 (22%)	38 (76%)	50
ADC	4 (8%)	09 (18%)	37 (74%)	50

p = 0.30

Survival rate

The mean survival rate was 7.7 ± 9.5 months for patients with SCC and 8 ± 10.9 months for patients with ADC.

Discussion

Retrospective demographic, nutritional and clinical data of 50 patients with SCC and 50 with ADC, treated in BUH from 2007 to 2012, were analyzed comparatively.

Both groups presented a greater incidence in men (96% in SCC and 86% in ADC), but there was no significant difference (p = 0.08) between the groups. The greater incidence of EC in men regardless of histological type has been reported by various investigators[1,6].

Esophageal cancer incidence is greater in individuals over 50 years of age due to the prolonged action of aggressive factors[6]. In the present study, the mean patient age was 60.3 ± 10.6 years (for SCC) and 62 ± 11.5 years (for ADC) without difference between them (p = 0.31). Dietz *et al*.[29] reported a mean SCC patient age of 69.4 years, higher than to that observed in this study. Tercioti-Junior *et al*.[30] investigated 103 patients with ADC and found a mean age of 56.98 ± 10.28, an age lower than that reported in our study.

Concerning race, we have observed a statistical prevalence of SCC in black patients and ADC in White patients (p = 0.002), which agrees with literature reports[20,21]. Brown *et al*.[31] attributed the high incidence of SCC in black men to various factors, the major ones being high ethylism, tabagism, and low vegetable and fruit ingestion together with low social economic level.

Regarding nutritional condition, the ADC BMI (21.4 ± 5.8 kg/m^2) was higher than in SCC (18.8 ± 3.5 kg/m^2), with a statistical significance (p = 0.007). Furthermore, we have found that 30% of the ADC patients were overweight or obese (BMI > 25 kg/m^2), while in SCC the incidence of overweighting was only 6% These results corroborate the hypothesis that a greater incidence of ADC in western countries is related to obesity[18,22,24].

Hongo *et al*.[20] reported that in countries with a greater incidence of ADC like United States, the daily energy intake is greater than in countries like Japan where ADC is rather rare. Thus, while in the United States the daily energy intake is 3695 calories, in Japan, it is 2750 calories. As a consequence of these eating habits, the authors say that in Japan only 1.8% of the population is obese, while in the United States 30.1% is.

Another parameter investigated in the nutritional evaluation, percent of weight loss (% WL) was not statistically different between the groups (p = 0.13). In our study, a % WL greater than 10%, indicative of severe malnutrition[27], was observed in 88% of the SCC patients and in 82% of those with ADC. These findings indicate that the lesion causes esophageal obstruction in both types of tumor and restricts food ingestion.

Under analysis, the lifestyle of SCC and ADC patients was significantly different. The length of time of ethylism and tabagism was significantly higher in SCC patients. Furthermore, associated ethylism and tabagism (Table 6) was more evident in SCC patients with a statistical significant difference. According to Lin *et al*.[4], ethylism and tabagism have a synergic effect in EC and the risk depends on exposure length, which was also observed in this study. Wheeler and Redd[21] reported a greater tobacco carcinogenic activity in EC for tar aromatic hydrocarbons and volatile nitrosamines.

Ethylism is also a risk factor, with the risk increasing with the amount of drinks consumed[21]. The action mechanism remains uncertain and various theories have been proposed, such as mucosa irritation, increased susceptibility to other carcinogens, in addition ensuing dietary deficiency[21].

Of the 50 patients with ADC from the present study, 11 (22%) were abstemious (Table 6) and 9 had Barrett Esophagus (Table 7). Thus, we may confirm that BE is an important risk factor for ADC, as previously demonstrated by various authors[10,15]. Tabagism alone was a more evident risk factor in ADC patients (22%).

Megaesophagus is another benign esophageal condition that adds to the malignancy esophageal risk, since it causes chronic irritation to esophageal mucosa due to stasis. In this study, two SCC patients presented chagasic megaesophagus.

Case-control studies conducted in Brazil have demonstrated that other factors may contribute to EC in addition to ethylism and tabagism, such as excessive pepper intake, intake of wood stove cooking and ingestion of high-temperature yerba mate[6,29,32].

Better treatment results of EC patients may be achieved with early diagnosis, with endoscopic follow-up of risk patients and orientation by health professionals for quitting smoking, restriction of alcoholic drink intake and of high temperature drinks and foods that may cause chronic irritation to the esophageal mucosa.

Conclusions

Being Black, excessive intake of alcoholic drinks and smoking are risk factors for squamous cell carcinoma;

Obesity, being White, smoking and Barrett's esophagus are the main risk factors for esophageal adenocarcinoma.

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