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Research Article

Epidemiology and Trend of Oesophageal Cancer in Santiago de Cuba

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Abstract

The incidence of oesophageal cancer varies significantly among different regions of the world and even within countries. More than 600 000 patients are diagnosed with oesophageal cancer worldwide each year. The aim of this research is to describe the epidemiological characteristics in the reference population and to identify the differential magnitude of incidence of patients with oesophageal cancer in the population, according to histological type. An observational, descriptive and cross-sectional study was conducted out in a first methodological stage and longitudinal one in a second(trend). For the analysis of the problems detected, the time period was from January 2011 to December 2020, and a sample of 197 patients was selected for the trend analysis. For the characterisation of the referred population, according to variables of interest, a subsample of 195 patients discharged from the hospital was selected, which included only the histological types of interest for the study: oesophageal adenocarcinoma and squamous cell carcinoma. Squamous cell carcinoma reported the highest percentages: 78.2%, but despite this, there was a slightly downward trend for this histological type and a slightly upward trend for oesophageal adenocarcinoma. The municipality of Santiago de Cuba registered the highest figures for both adenocarcinoma and squamous cell carcinoma: 40.3% and 26.8% respectively, with the highest number of cases in San Luis. The incidence of the disease was higher in patients over 50 years of age, with a high incidence in males and mixed race patients, although there were reports of subjects younger than 40 years old. The joint effect of tobacco and alcohol consumption showed a strong association for the development of oesophageal adenocarcinoma, with a Cramer's coefficient of 0.67.

Keywords: oesophageal adenocarcinoma, oesophagus cancer, squamous cell cancer

Abbreviations

WHO: World Health Organisation; ESCC: Esophagus Squamous Cell Carcinoma; EAC: Esophageal Adenocarcinoma; HR: Hazard Ratio; IARC: Agency for Research on Cancer; EB: Barrett´s Esophagus; GERD Gastro-oesophageal Reflux Disease; HDI: Human Development Index

Introduction

Cancer represents one of today's major health problems. The number of people suffering from cancer is alarming. According to the World Health Organisation (WHO), it is the second leading cause of death in the world, with a high mortality rate in underdeveloped countries. Only in 2018, 18.1 million new cases of cancer were reported, and GLOBOCAN estimates indicate that this number will increase over the next two decades, and could reach 29.5 million by 2040 [1,2].

Oesophageal cancer (EC) occupies an important place among malignant neoplasms, due to its high lethality and dismal prognosis. Its incidence varies significantly among different regions of the

world and even within a single country, which has been related to different risk factors [3,4]. More than 600 000 patients are diagnosed with oesophageal cancer worldwide each year; 604 100 new cases were diagnosed in 2020, and its lethality is so high, that it is considered the sixth leading cause of cancer deaths, according to the GLOBOCAN 2020 report [5-7].

According to reports by various authors [8-11], it is a nosological entity with a high lethality rate, affecting an increasing number of individuals, with serious implications for life quality and high healthcare costs, and its two main histological types are esophageal squamous cell carcinoma (ESCC) and oesophageal adenocarcinoma (EAC), which account for around 90% of all cases of EC. Their presentation in advanced stages compromises patient survival and makes therapeutic management difficult, leaving palliative modalities as virtually the only option for a large number of patients.

Despite the fact that oesophageal cancer is a well-studied nosological entity, and that there are national reports on the subject, in Santiago de Cuba there is still insufficient knowledge about its epidemiological and clinical-surgical characteristics, as well as about the differential magnitude of the main histological types in our province, mainly due to the scarcity of publications on the subject. The aim of this research is to describe the epidemiological characteristics in the reference population, and to identify the differential magnitude of incidence in the oesophageal cancer patient population, according to histological type.

Materials and Methods

General characteristics of the study

An observational, descriptive and cross-sectional study was conducted in a first methodological stage, and longitudinal in a second one (trend), to identify histological differences in patients with oesophageal cancer, as well as the attributes referred to the epidemiological, clinical and surgical treatment dimensions. For the analysis of the problem under research, the time period from January 2011 to December 2020 was selected.

Population and sample

The population consisted of all patients with a confirmatory histological diagnosis of oesophageal cancer > 18 years of age. A sample of 197 patients was selected for trend analysis. For the characterisation of the referred population, according to variables of interest (epidemiological, clinical, surgical treatment and evolutionary), a subsample of 195 patients was selected, discharged from the hospital institution, with available clinical history and complete empirical data to achieve the aims. This subsample includes only the histological types of interest for the study: oesophageal adenocarcinoma and squamous cell carcinoma.

Exclusion criteria

- Siewert - Stein II and III oesophagogastric junction tumours.
- Histological diagnosis other than oesophageal adenocarcinoma and squamous cell carcinoma.

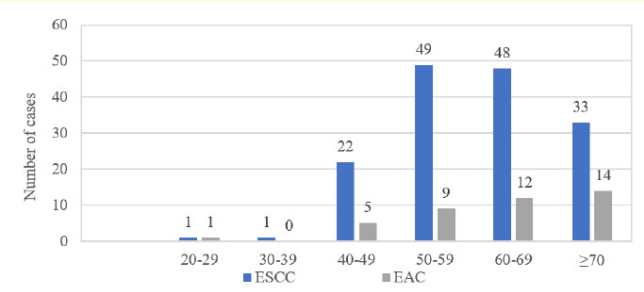
Techniques and procedures

Primary, secondary and tertiary sources were consulted; likewise, articles published mainly in the last 10 years in journals indexed in Index Medicus, as well as in Cuban Medical Journals were reviewed. PubMed, ClinicalKey, ClinicalTrials.gov, Lilacs, EBSCO, Hinari and Scielo databases were used, as well as search engines such as GOOGLE SCHOLAR. The strategy used was based on the combination of keywords such as: "oesophageal cancer", "adenocarcinoma", "oesophageal adenocarcinoma", "squamous cell carcinoma", and their equivalents in Spanish; with no language limit. Data were processed and analysed using summary measures for each variable. Standard deviation and mean were used for quantitative variables and percentage, and Cramer's V coefficient for qualitative variables. The analysis was performed with the statistical software SPSS for Windows version 20.0.

Results and Discussion

Age and Sex

At diagnosis, the age of the patients ranged from 22 to 92 years, with a range of 71 years and a mean age of 61.9 years [σ ± 11.8; 95% CI: 60.2-53.6], quite close to those reported by Castellanos., *et al.* [9]. and Pedram., *et al.* [12]. of 62.8 and 61 years, respectively. The mean age for ESCC was 60.9 years [σ ± 11.6; 95% CI: 59.0-62.7]. and 63.4 [σ ± 12.7; CI: 59.5 - 67.4]. for EAC. The highest number of cases occurred after the age of 50 years, with the highest percentage between 60 - 69 years (84.6%). We observed a steady increase from the age of 50 years for both histological types, with a decrease from the age of 70 years for ESCC.



Graph 1: Distribution according to age groups and histological variants.

Graph 1 shows that the frequency of ESCC cases was higher in the 50-59 years subgroup (49 subjects) 31.8% of all ESCC cases; however, the difference with the next age group for this same histological variant was only 0.6%. For EAC the highest percentage volume was found in > 70 years (14 subjects; 34.1%; n = 41). The report of ESCC and EAC in patients > 70 years was significant 21.4% and 34.1% respectively. Spicer [13]. agrees with our study in this aspect, while Locke's [14]. results differ.

In the series, 47 subjects with EC (24.8%; n = 195), were older than 70, which differs from the incidence in this age in countries such as China and Iran, where the disease is endemic. However, the General Practitioners Research Data Base, [15]. which studied 2 million inhabitants in the UK, found that, of the 909 diagnoses of EC, 40% were aged 70-79 years.

According to most authors [8,16,17]. the incidence of EC is higher from the 5th decade of life onwards. According to Gómez-Urrutia [18]. the usual age of presentation is between 55 and 70 years old-,and it is rare in patients under 40 years of age. In our investigation, there was a clear predominance from the age of 50 and only 3 cases occurred below the age of 40 (1.5%; n = 195). On the other hand, the American Cancer Society states [19]. that the probability of developing EC disease increases with age, and that less than 15% of cases occur in those under 55 years. In our investigation, 26.2% of cases were reported in subjects younger than 55, which differs from the reports of this organisation, and is evidence of an earlier presentation of the disease.

Several studies held in our country are in agreement with our research in suggesting a higher frequency of the disease from the seventh decade of life onwards. Estopiñan., *et al*. [20]. reported 56.2% (n = 59); Hidalgo Herrera., *et al*. [21]. reported 58.1% (n = 62) and Nazario., *et al*. [22]. reported 52.9% (n = 51). Cuban Health Statistical Yearbooks show the highest incidence rates in the population > 60 years old; the 2020 yearbook [23]. reports that in 2017, 455 new cases (n = 731) of EC were diagnosed in that same age range, for a rate of 43.7.

	ESCC				EAC				Total	
Decades	(n = 154)				(n = 41)					
	F	%	M	%	F	%	M	%		%
20-29	0	0	1	0.8	0	0	1	3.2	2	1
30-39	0	0	1	0.8	0	0	0	0	1	0.5
40-49	3	12	19	14.7	1	10	4	12.9	27	13.8
50-59	4	16	45	34.9	3	30	6	19.4	58	29.7
60-69	6	24	42	32.6	3	30	9	29	60	30.8
≥70	12	48	21	16.3	3	30	11	35.5	47	24.1
TOTAL	25	100	129	100	10	100	31	100	195	100
σ ± 11.8 IC [60.2-63.6].										

Table 1: Distribution according to age groups, sex and histological variants.

Codipilly and Sawas, [24]. referring to EAC, state that they have observed increased incidence in young people from 1975 - 2015, with an annual 2.9% variation, and presentation in more advanced stages, compared to older patients. In our study we had 2 patients younger than 39 years with EAC, who were categorised as stage IIIA and IV.

Among women with ESCC, the highest number of cases was recorded in those older than 70 years (12 cases; 48.0%), with 3 patients > 80 years and one patient over 90 years of age. The mean age of women with ESCC was 67.6 [σ ± 13.6; 95% CI: 65.4 - 69.8]. Among men with ESCC 34.9% were aged 50 - 59 years; 8 subjects were older than 80 years and one was 28 years. The mean age of men with ESCC was 60.3 [σ ± 10.7, 95% CI 58.6-62.0]. The male to female ratio was 5.2/1 for EC overall and the same for ESCC.

Female patients accounted 24.4% of all the diagnosed cases of EAC, with a mean age of 64.9 [σ ± 12.3; 95% CI: 61.0-68.8]. The

male sex presented 31 cases of EAC with a mean age of 62.9 [σ ± 12.9; 95% CI: 58.8-66.9]. and the male/female ratio was 3.1/1 for EAC.

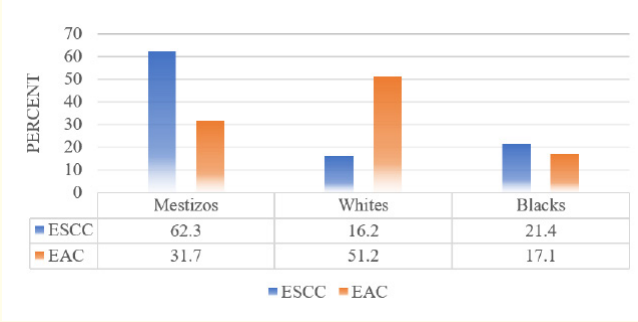
The literature [12,25-27]. reports higher frequency of CE in male patients, with the male/female ratio varying according to geographical areas; there are areas where it can be as high as 14/1 or as low as 1/1 or less, as is the case in Mongolia, some regions of Iran and northwest China. Studies in Iran found low ratios; one in Golestan [12]. reported 0.84/1 average age of 61, while the other one [28]. showed a ratio of 1/1. A study in Sistan and Baluchestan [27]. even reported that SC was the second most common disease in women in that region, and the fourth most common in men. These in-country variations in endemic areas seem to be due to multiple factors.

In Western Europe and much of our hemisphere, this proportion does not show as much variability, and there is a marked male predominance. In low EC incidence areas in the US and France, the ratio is 4/1, very similar to ours, which was 3.8/1. As for the overall ratio of the two main histological types Arnold., *et al*. [29]. reported 2.7/1 for ESCC and 4.4/1 for EAC, ours being much higher (5.2/1) than the former, and lower than the latter (3.8/1).

In table 1 above, Cramer's V coefficient was applied to assess the association between the variables represented in the table; the analysis of this coefficient was performed for each histological type, obtaining 0.29 for ESCC, determining a moderate association; and for EAC 0.14 with a weak association.

Skin colour

Skin colour, ethnic groups, as well as certain habits and lifestyles are related to EC [20,31]. In graph 2 it is stated that the highest percentage weight (55.9%) is for mestizos, representing 62.3% and 31.7% of the subjects with ESCC and EAC respectively. For EAC, the prevalence was for white-skinned patients, representing51.2%. This predominance of mestizos observed in the series is understandable, given the interraciality existing in our country. According to the 2012 population and housing census, [32]. Santiago is the province with the second highest mestizo population after Guantánamo, with 60.2% of mestizos. Nazario., *et al*. [22]. found that 58.8% of the individuals studied were mestizos. Meanwhile, Carballosa., *et al*. [6]. noted a higher number of white patients, revealing a 47.3%.



Graph 2: Distribution according to skin colour and histological variants.

ESCC is more common in the black population, with a higher incidence in men of African origin. The study by Ashktorab., *et al*. [31]. in the US revealed that ESCC accounted for 26% of the non-Hispanic whites, and 80% in marily in white patients, most of whom have a history of gastro-oesophageal reflux disease (GERD) or Barrett's oesophagus (BE), which are considered the most significant entities associated with SCC. In the presenblacks, while among Hispanics it was 41%. Moreover, SCC occurs prit series, we found that all 7 subjects with a history of GERD and 3 with BE were white-skinned.

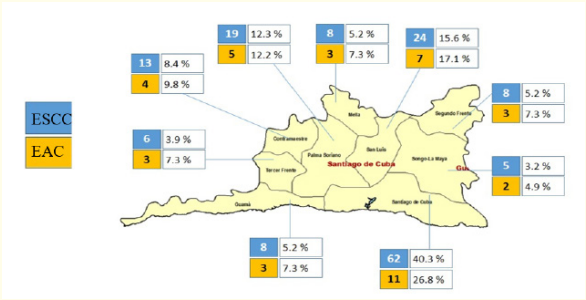
Laszkowska., *et al*. [30]. report that, of the cases with EAC, the incidence was higher among white people (89.0%), while black patients accounted for only 2.4%. According to Ashktorab., *et al*. [31]. the US reports 68% of the cases of EAC in white patients and 15% in black ones. Similar results were found, although not as markedly different as those of Laszkowska. In our study white and black individuals with EAC accounted for 51.2% and 17.1% respectively.

Municipalities of Residence

The highest percentage of the cases occurred in the municipality of Santiago de Cuba, for both histological types: ESCC (40.3%; n = 154) and EAC (26.8%; n = 41), followed by San Luis ESCC (15.6%); EAC (17.1%) and Palma Soriano ESCC (12.3%); EAC (12.2%). It is noteworthy that San Luis, with a lower population density than Palma Soriano and Contramaestre, [32,33]. had higher EC figures, even though most of the patients in the three municipalities had similar risk factors (smoking and alcohol consumption). During questioning 13 patients from San Luis reported drinking well wa-

ter, but this was not analysed by the authors to confirm the presence of nitrates or nitrites which, in other regions, [34-36]. have been associated with EC.

When comparing the EC ratios between Santiago and San Luis, it is observed that it is 2.3/1, i.e., for every patient diagnosed in San Luis, 2.3 cases are diagnosed in the head municipality. Particularly, for each histological subtype it behaves in a similar way, being 2.6/1 in the case of ESCC, and 1.6/1 for EAC. In the case of the latter, the difference is minimal between the two municipalities.



Graph 3: Distribution according to municipality of residence and histological variants.

This graph is quite illustrative in terms of the geographical distribution of our caseload, but we did not find any studies, in our country or in the province, with which it could be compared. In other parts of the world, mainly in China, studies have been developed where comparisons are conducted in regions within the same country as in Iran, but this is not the case in Cuba, where research in different territories does not compare the distribution of EC among municipalities. Particularly in Santiago de Cuba, the authors have no reference to studies that address this issue.

In the series by Nazario., *et al.* [22]. as well as in the research of Carballosa., *et al.* [6]. both from the east of the country, a higher incidence was found in the urban population. In our study, we decided not to assume the categorisation of rural or urban, since despite being registered as such in the medical records, there is bias in the data collection. This is because the admission staff often records the municipality of origin in the home address, without specifying in detail that could help to establish urban or rurality. Moreover, during the preparation of the psychosocial history, many doctors assume the origin of any municipality other than Santiago as a rural area, without taking into account the criteria for human settlements used by the 2012 population and housing census [32].

Tobacco consumption

Smoking is associated with several types of neoplasms. Its effect on the development of both EC has been extensively studied, and according to Dong [37]. it is a stablished risk factor for both ESCC and EAC. In our series, tobacco consumption was significant for both histological types: 87.7% of ESCC patients, and 85.4% of EAC subjects had some form of tobacco use, and only 12.8% of the sample did not smoke, while 58.5% (126 subjects; n = 195) were regular smokers. Table 5 shows the study subjects according to their smoking habits, taking into account the criteria established by the WHO [38]. For both histological types, patients reporting daily consumption of at least one cigarette in the last 6 months predominated (66.2% with ESCC and 58.5% with EAC).

Tobacco comsumption	ESCC		EAC	
	No.	%	No.	%
Habitual smoker	102	66.2	24	58.5
Occasional smoker	13	8.4	1	2.4
Passive smoking	9	5.8	6	14.6
Ex-smoker	11	7.1	4	9.8
Non-smoker	19	12.3	6	14.6
Total	154	100	41	100

Table 2: Distribution according to tobacco use and histological variants.

In a multicentre study in the Netherlands, [39]. a positive independent association between frequency, duration and yearly consumption of cigarette- with ESCC and EAC was demonstrated, and current smokers were found to have a relative risk of 2.63 for ESCC. Ishiguro, Zendehdel and Tran, cited by Abnet, [40]. agree that both intensity and duration of exposure are relevant to the risk of ESCC transmitted by tobacco smoking. IARC studies, [15]. comparing smokers and non-smokers, found a relative risk for smokers to develop ESCC and ESCC of 2 - 5 and 1.5 - 2.5 respectively. While a case control study in Dafeng and Ganyu [41]. revealed that former and current smokers in the former city have a 1.93- and 2.42-times higher risk of developing EC than non-smokers, and 1.28 and 2.36 in the latter city.

Santell., *et al*. [8]. note that the risk of CE is five times higher among patients who smoke and the excess risk increases to almost 10 times among heavy smokers, and further state that this risk decreases significantly within a decade of smoking cessation.

Tobacco-specific nitrosamines and polycyclic aromatic hydrocarbons are believed to be the main carcinogens in tobacco. A cohort study in Shanghai [40]. found that Chinese smokers were exposed to fewer tobacco nitrosamines compared to American smokers. However, these researchers also reported that urinary N-nitrosonornicotine concentration was strongly related to ESCC risk, and inferred that this may be the causative agent in these tobacco smokers.

Alcohol consumption

Alcohol consumption has been described as one of the most important factors in the development of ESCC, but not for EAC. According to Santell., *et al.* [8]. the relative risk of EC increases with the amount of alcohol consumed and is approximately 1.8 times for five to eleven drinks per week and increases to 7.4 times for more than 30 drinks per week.

Alcohol consumption	ESCC		EAC	
	No.	%	No.	%
Total abstinence	8	5.2	3	7.3
Occasional use	38	24.7	32	78.0
Frequent use	108	70.1	6	14.6
TOTAL	154	100	41	100

Table 3: Distribution according to tobacco consumption and histological variants.

The subjects in this series have been according to Marconi's criteria [42]. 58.5% (114 subjects; n = 195) had frequent (heavy or pathological) consumption, being more significant among ESCC patients (70.1%; n = 154). Occasional use recorded in 35.5% (70 subjects; n = 195), for EAC, it represented 78.0% (32 subjects; n = 41). Only 5.6% (11 subjects; n = 195) did not consume alcohol. When determining the ratio between frequent drinkers for ESCC and EAC it was 18:1, showing a higher frequency of regular drinking among subjects who developed ESCC. However, the ratio between occasional drinkers is not so distant, since it is 1.2/1.

According to Abnet, [40]. authors such as Lin, Yu and Chen report that alcohol consumption increased the risk of ESCC by 1.6 to 5.3 times in Asian countries, including China, Iran, Japan and India; and for Africa and South America, Segal, Pacella and Castelletto report an increase of approximately 3 times. Whereas in areas with low incidence rates for ESCC, the association between alcohol and ESCC is stronger, with approximately 6-fold increased risk in Europe and 9-fold increased risk in North America.

Matejcic [43]. reports that a prospective investigation included 97 incident ESCC subjects in the US and showed that regular alcohol drinkers had a hazard ratio (HR) equal to 4.93 [95% CI: 2.69-9.03]. compared to occasional drinkers. Matejcic himself reports that these results were reaffirmed by two cohort studies in China and Europe, which showed a relatively higher risk among regular drinkers, HR = 2.02 [95% CI: 1.31-3.12]. and HR = 4.61 [95% CI: 2.24-9.50].

Joint effect of tobacco and alcohol consumption

Alcohol and tobacco use are usually complementary behaviours, and it is difficult to isolate their individual effects in an outcome in observational studies [43]. Case-control studies have demonstrated the independent and synergistic effects of alcohol and smoking. Alcohol alone, as reported by Arango, [44]. does not greatly increase the risk of ESCC, and in the case of EAC it is not considered a major risk factor. However, when it is associated with smoking, its effect is enhanced and the risk increases up to sevenfold.

Table 4 shows the association found in patients with ESCC in our series, 76 regular smokers frequently consumed alcohol. Of the passive smokers, ex-smokers and non-smokers, 5, 8 and 13 respectively regularly consumed alcohol. Table 5 shows the same association for ACE cases, where 22 regular smokers were occasional alcohol consumers. Determining the Cramer's V coefficient to assess the degree of association between tobacco and alcohol consumption and their effect in producing CE, it was 0.67 for EAC, establishing a strong association, while for ESCC this relationship was weak.

Yan., *et al*. [45]. analysed the joint effects of alcohol and tobacco for ESCC risk, finding that the association of these compared to non-habitual smokers and non-alcohol drinkers was statistically significant (p = 0.003). This study showed that the excess risks of

Tobacco consumption	Alcohol consumption			Total
	Total abstinence	Occasional use	Frequent use	
Habitual smoker	4	21	76	101
Occasional smoker	1	6	6	13
Passive smoking	2	2	5	9
Ex-smoker	0	3	8	11
Non-smoker	1	6	13	20
Total	8	38	108	154

Table 4: Association of tobacco/alcohol use for squamous cell carcinoma.

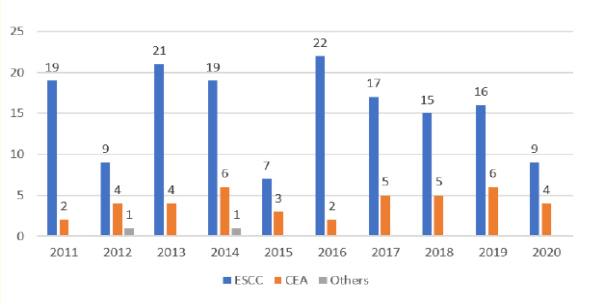
Tobacco consumption	Alcohol consumption			Total
	Total abstinence	Occasional use	Frequent use	
Habitual smoker	0	22	2	24
Occasional smoker	0	0	1	1
Passive smoking	0	4	2	6
Ex-smoker	3	0	1	4
Non-smoker	0	6	0	6
Total	3	32	6	41

Table 5: Association of tobacco/alcohol use for adenocarcinoma of oesophagus.

ESCC increased monotonically among current smokers, with decreasing age at starting to drink alcohol. These same authors point to alcohol and tobacco as the most important risk factors in Western countries, which together account for almost 90% of the population attributable fraction. However, the contribution of these two factors, in areas considered high risk for ESCC, is weaker.

Trend

The highest percentage of cases in our series corresponded to ESCC with 78.2% (154 subjects; n = 197), a similar finding reported in Cuba by Nazario [22]. and Estopiñan [20]. Internationally, this phenomenon varies mainly due to the increase of SCC cases in Western countries. In Asia, reports continue to show ESCC as the main histological type [7,26,46]. IARC itself estimated [40]. that in 2012 the numbers of patients with EC was 450 000, with 88% ESCC and 12% ESCC. The African research [25,47-49]. also reveals the preponderance of ESCC, in Uganda for example the ESCC/ECC ratio is 13/1, and similar in Ethiopia. In our hemisphere Beddenne., *et al*. [11]. in France and Taruselli., *et al*. [50]. in Uruguay report a similar behaviour of these histological forms.



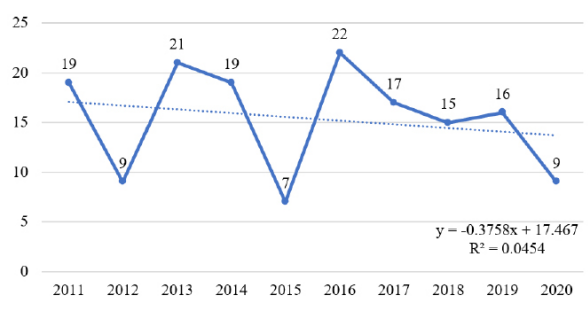
Graph 4: Distribution of cases by year according to histological variants.

Regarding ESCC, multiple publications [3,51,52]. allude to the increase experienced in Western countries, with a higher incidence in those with a high or very high human development index (HDI), where the incidence of ESCC has decreased, perhaps related to changes in the main risk factors in these populations. The countries that stand out for this are mainly the US, UK, Canada, Australia and several northern European nations, which is not consistent with most of the reports from Cuba or with the results of this research.

Edgren., *et al*. [53]. report an increase in EAC, with an average annual increase of 3.5% in Scotland and 8.1% in Hawaii, with similar increases in men and women, in the period 1960-1990. Another study with which we differ is the analysis of the Hospital Juárez in Mexico, [18]. in which figures for EAC (39.4%) were relatively higher than those for ESCC (27.7%). In the case of Cuba, only one study, belonging to the "Carlos J. Finlay" Hospital, [21]. reported a higher number of cases for EAC.

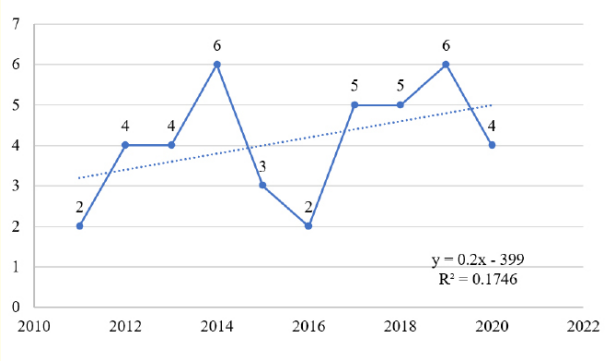
As can be seen in graph 5, despite ESCC being the most frequent in the decade analysed, it has a discreet downward trend, a phenomenon that is experienced in Western countries with a high or very high HDI, where there has even been a reversal of the ESCC/EAC ratio, with ESCC in some countries surpassing the number of cases in several countries, This is related to the high rates of obe-

sity, the increasingly common occurrence of GERD, the decrease in the consumption of alcohol and tobacco in these countries, and the better socio-economic conditions compared to countries with low or moderate HDI. Despite this, Abnet [40]. suggests that ESCC is unlikely to decrease even in the presence of low incidence rates, given the ageing population in Western countries, as this population is the one most affected by ESCC.



Graph 5: Trend of Squamous Cell Carcinoma by year.

Graph 6 shows the trend that EAC followed during the decade of study, the linear representation of the trend exposes that EAC experienced a slight rise with a maximum peak in the year 2014 and 2019. If we compare the five-year periods 2011-2015 and 2016-2020, we see that in the latter there was a slight increase compared to the preceding five-year period. Previous studies [18,21,53]. also refer to the increase in EAC in their results.



Graph 6: Trend of Esophageal Adenocarcinoma by year.

Conclusions

Oesophageal cancer continues to be a disease that occurs later in life with a significant predominance in the male sex and in our territory there is a discreet trend towards an increase in oesophageal adenocarcinoma, although squamous cell carcinoma continues to have a higher incidence.

Tobacco and alcohol consumption are associated with cancer, with a strong association being established between the combination of smoking and alcohol consumption.

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