Supraglottic and Glottic Carcinomas. Study of the Incidence in the Last 31 Years

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Introduction: Laryngeal carcinoma is a common neoplasia in our country. It is well-known that the supraglottis is more frequently involved in Mediterranean countries. We present our results on the incidence of neoplasias affecting supraglottis and glottis and we find a change in the normal trend.
Objective: To study the incidence of glottic and supraglottic tumours in our hospital over the last 31 years. We also analyze risk factors such as smoking and alcohol in the population of the Valencian Region.
Patients and methods: We performed a retrospective review of 991 patients diagnosed as having carcinomas of the glottis and supraglottis between 1974 and 2005. The epidemiological data about the consumption of tobacco and alcohol in the population of the Valencian Region, Spain, are obtained from descriptive epidemiological studies (Health Statistics and the 2003 National Health Survey).
Conclusions: With a total of 548 carcinomas of the glottis and 443 of the supraglottis, we find a change in the incidence maintained since 1990, with statistically significant differences (*P*=.0056). Thus, we can state that the glottis is more frequently affected than the supraglottis. Changes in the consumption of tobacco and alcohol cannot explain this current change.

Key words: Incidence of laryngeal carcinoma. Supraglottis. Glottis. Epidemiology of laryngeal carcinoma.

Carcinomas supraglóticos y glóticos. Estudio de la incidencia en los últimos 31 años

Introducción: Los carcinomas de laringe son una neoplasia frecuente en nuestro país. Por todos es conocido que en los países mediterráneos predomina la localización supraglótica sobre la glótica. Hemos estudiado la incidencia en nuestro medio de ambas localizaciones y hemos comprobado una inversión.
Objetivo: Estudiar la incidencia de los tumores glóticos y upraglóticos en el Hospital Universitario Dr. Peset en los últimos 31 años. También se analizan los hábitos tóxicos de la población de la Comunidad Valenciana relacionados con la aparición de este tipo de neoplasias.
Pacientes y método: Realizamos un estudio retrospectivo de 991 pacientes diagnosticados de carcinomas glóticos y supraglóticos desde 1984 a 2005. Los datos epidemiológicos respecto al consumo de tabaco y alcohol en la población de la Comunidad Valenciana se obtienen a través de estudios epidemiológicos descriptivos de ámbito nacional (Estadísticas de Salud y Encuesta Nacional de Salud 2003).
Conclusiones: Con un total de 548 carcinomas de localización glótica y 443 de localización supraglótica, hemos observado una inversión en la incidencia desde el año 1990 que se mantiene hasta la actualidad, con diferencias estadísticamente significativas (p=0,0056). Por lo tanto, se puede afirmar que actualmente la incidencia de tumores glóticos es mayor que la de los supraglóticos en nuestro medio. Los cambios en el estilo de vida de nuestra población actualmente no permiten explicar este cambio.

Palabras clave: Incidencia del cáncer laríngeo. Supraglotis. Glotis. Epidemiología del cáncer laríngeo.

INTRODUCTION

Laryngeal cancer is one of the most frequent head and neck neoplasias and the second most frequent one found in the airways, following lung cancer. It represents between 1% and 2% of all malignant tumours in the body.[1]

Both the general incidence and the incidence by location (supraglottis, glottis, subglottis) have geographic variants. The glottis is classically affected more often than the supraglottis, except in certain Latin American and Mediterranean countries, such as ours, in which supraglottic localization is found more frequently.[2-6]

The factors most closely related with the appearance of laryngeal cancer are smoking and alcohol consumption, with a dose-dependent multiplicative relation.[7,8]

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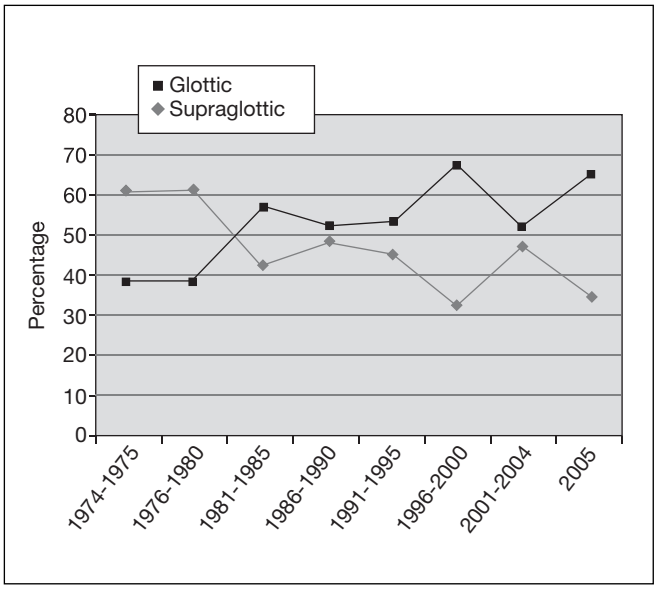

Figure 1. Percentage of glottic and supraglottic tumours in the period studied.

A link has also been seen between laryngeal cancer and exposure to industrial gases (aromatic and polycyclic hydrocarbons, metallic dust, cement, and varnishes), among people who work with wood, are infected with HPV, have a diet poor in fruit, dairy products and vegetables,[9] or suffer from a mutation of the *p53* gene and pharyngolaryngeal reflux.[8,10]

There are also gender-based differences: it is the neoplasia with the highest male-to-female ratio in most populations.[11] The likelihood of a multifactorial origin is currently seen as the most consistent.

The aim of this study is to evaluate the incidence of supraglottic and glottic localizations in our country as well as to revise the literature on the subject. Possible lifestyle changes are also analyzed regarding the main risk factors for laryngeal cancer (tobacco and alcohol) as they may justify changes in its incidence.

PATIENTS AND METHOD

We present a retrospective study of 991 cases of glottic and supraglottic carcinomas diagnosed at the Dr. Peset University Hospital in Valencia, over a period of 31 years, from January 1974 to December 2005.

The TNM staging system used is that proposed by the AJCC-UICC in 2002.

The epidemiological data of the population came from "Estadísticas de Salud"[12] and "Encuesta Nacional de Salud"[13] ("Health Statistics" and "National Health Survey") published, respectively, by the Directorate-General for Public Health at the Ministry of Health and Consumer Affairs and the National Statistics Institute.

For the statistical analysis, we used SPSS version 12 and EpiDat 3.1.

RESULTS

Patient Information

The mean (standard deviation) of the sample age is 61 (10) years old (interval, 32-88 years).

Regarding gender, of the 991 patients, 972 are male and 19 female. Therefore our male-to-female ratio is 50:1.

Information About Laryngeal Tumours

We diagnosed a total of 991 cases of intrinsic laryngeal carcinomas (excluding those with a subglottic origin), with 548 carcinomas located in the glottis (55.29%) and 443 in the supraglottis (44.7%).

If we group together the number of tumours we diagnose in both localizations in each 5 year period and calculate the percentage they represent of the total (the results are shown in Figure 1), we confirm that glottic tumours are diagnosed more frequently from nineties on and that this trend is steadily maintained. After a statistical analysis using the χ^2 test for independent variables using that date as the cut-off point, we see statistically significant differences for both glottic and supraglottic locations (P=.0056).

We have performed a linear trend analysis by a curvilinear estimation regression model. With glottic tumours, an increasing linear trend is seen in both the total number of glottic tumours (Figure 2A), and as a percentage of supraglottic ones (Figure 2B), and of the total, all statistically significant (P<.005).

Regarding supraglottic tumours the information is largely dispersed, which means it is not significant (P=.24), with a seasonal or slightly increasing trend (Figure 2D).

The clinical tumour staging done at the moment of diagnosis is shown in Table. When the tumours are grouped together according to the date of diagnosis (before or after 1990) only 3.22% of the supraglottic tumours were diagnosed at T1 stages before 1990, while 15.55% were diagnosed at that same stage after that date. These differences are statistically significant (P=.0000). Regarding glottic tumours before 1990, 56.88% were diagnosed in the T1 stage, and 64.81% were diagnosed after that. This difference is close to being statistically significant (P=.073) (Figure 3).

As for the most frequent histopathological type, 99.2% are squamous cell carcinomas and there are 11 cases (1.1%) of the verrucous variant. The remaining 0.8% is non-squamous cell histopathologies (giant cell, mucoepidermoid, rhabdomyosarcoma, and adenoid cystic tumours).

Epidemiological Information Regarding Tobacco Use

We analyzed tobacco use in the Valencian Region by people over 16 years of age. The first epidemiological studies carried out by the Directorate-General for Public Health (Ministry of Health and Consumer Affairs, MSC) and found in the "Health Statistics" publication for 1987 provide us with the following information:

– Non-smokers: 49.9%
– Regular smokers: 37.5%
– Ex-smokers: 11.3%

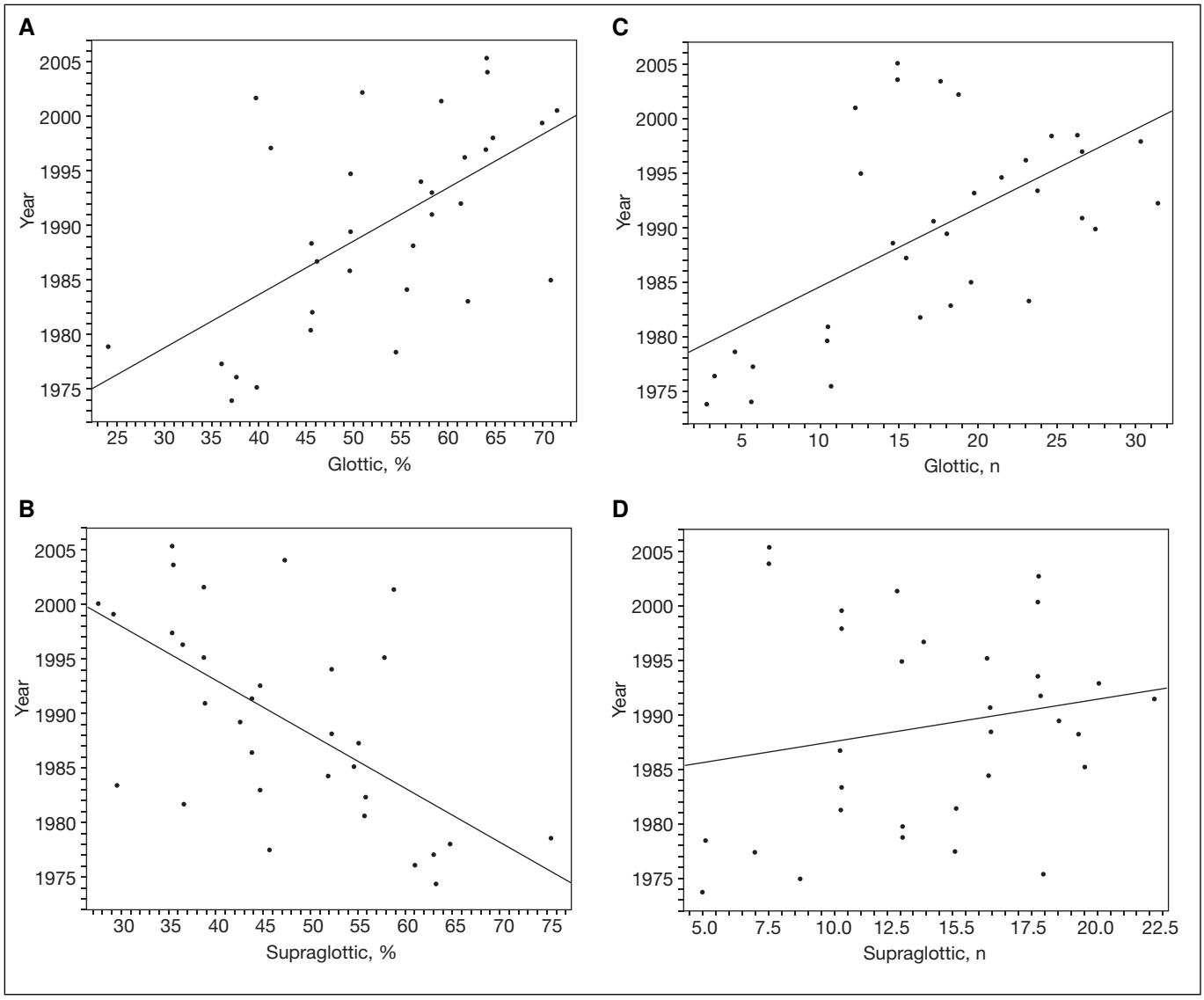

Figure 2. Regression analysis through a linear estimate of the proportion of glottic tumours (A), the proportion of supraglottic tumours (B), the total number of glottic tumours (C), and the total of supraglottic tumours (D).

We will consider the last 2 groups to be at risk, which means that 48.8% of the population over 16 years of age is at risk, while approximately 50% is not.

The most recent epidemiological studies on tobacco use are from 2003 and were done by the National Statistics Institute through the "National Health Survey." Besides smokers, non-smokers, and ex-smokers, a fourth group comprising occasional smokers is included:

– Non-smokers: 49%
– Regular smokers: 31%
– Ex-smokers: 17%
– Occasional smokers: 3%

If we also take into account occasional smokers as being at risk then 48% of the population is at risk, and 52% is not. The differences are not statistically significant (P=.2311).

Clinical Staging of Glottic and Supraglottic Tumours

	Glottis	*Supraglottis*
T1	335	48
T2	121	222
T3	81	140
T4	11	33

Epidemiological Information Regarding Alcohol Use

As in the previous case, the oldest data come from the same 1987 source. The following parameters are analyzed:

– Non-drinkers: 35%
– Occasional drinkers: 13%
– Moderate drinkers: 45%

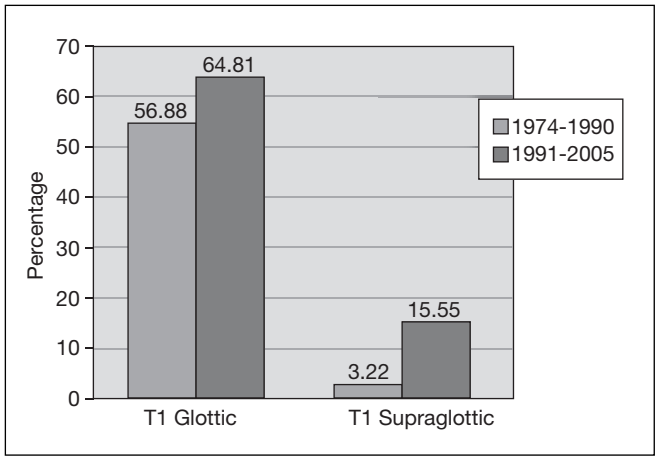

Figure 3. Percentage of glottic and supraglottic tumours diagnosed at stage T1 before and after 1990.

– Heavy drinkers: 4%
– Alcoholics: 3%

Considering the first 2 groups as not being at risk and the rest as being at risk, the percentages are 48% and 52%, respectively.

The most recent information regarding alcohol consumption is from 2003. The source is the National Statistics Institute (MSC) which, through the "National Health Survey," asks people if they "consumed alcohol in the last 12 months" (60% say "yes" and 40%, "no") and "during their lifetime" (65% say "yes" and 35%, "no").

DISCUSSION

The predominance of supraglottic tumours over glottic tumours in Spain, as well as in other Mediterranean countries,[1-6] has changed over the last few years. Even though initially supraglottic carcinomas are more frequent than glottic ones, we can see that around the eighties (and lasting practically up to now) a change occurred and glottic neoplasias are now more frequent than supraglottic ones. At the same time the regression analyses show clearly progressive linear trends in the ratio of glottic to supraglottic tumours.

Other European authors coincide with what we have found in detecting this change in the incidence of the most frequent sublocations of laryngeal carcinomas. In Spain, in a 2005 study by Lechuga et al,[4] 60%-65% of cases with glottic localization can be seen over the preceding 10 years, with 30%-35% supraglottic tumours while the remaining 5% are subglottic, as opposed to the predominant supraglottic location seen from 1975-1994. In Finland[2] these epidemiological changes have been observed for a few decades now. In the records of patients treated at the Central University Hospital in Helsinki between 1936 and 1961, two-thirds of the tumours were supraglottic.[14,15] On the other hand, at the Central University Hospital in Turku, 60% of the tumours were glottic[16] between 1981 and 1990. Other records from hospitals such as the University Hospital in Tampere, also in Finland, show a progressive increase in the glottic to subglottic ratio between 1962 and 1966 (0.5:1) and 1987-1991 (1.9:1).[17]

As for the study of epidemiological factors linked with these neoplasias, one of the main difficulties we find is the lack of reliable epidemiological studies large enough to analyze the period under study. All this currently limits the possibility of establishing links between the changes found in the incidences of sublocations of laryngeal cancer and changes in the use of tobacco and alcohol as well as the dietary habits of the population. In addition, the epidemiological studies often do not compare exactly the same parameters.

With respect to tobacco use, we can see that among the analyses covering 1987 to 2002 the ratios of people at risk are stable at around 50% and the differences found are not statistically significant (*P*=.2311). The only noteworthy change would be the increase in the group of ex-smokers (11% in 1987 and 17% in 2002).

Regarding alcohol consumption, the 1987 survey showed 52% of the population was at risk, while in 2002 around 60% of those surveyed answered "yes" to the question "have you consumed alcohol in the last 12 months?" and "…during your lifetime?." From our point of view those questions are quite ambiguous and do not allow us to make reliable comparisons. Despite reaching statistically significant differences (*P*=.0000), we do not consider this relevant because the technique used has the limitation of being affected by the sample size and in both studies the sample is very large.

In a study conducted by the International Agency for Research on Cancer (IARC)[18] one of the main findings was the identification of 2 clinical entities, with differences in the risk of carcinogenesis from tobacco and alcohol. One entity comprised the supraglottis and hypopharynx, locations that come into direct contact with the food eaten. The other is the endolarynx, through which air passes (and thus tobacco smoke) but not food, which is diverted toward the oesophagus when the glottis closes during swallowing. The risk of alcohol carcinogenesis is much higher for the supraglottis (also for the hypopharynx) than for the endolarynx, while the risk associated with tobacco is slightly higher for the endolarynx.[19] As we have seen, it seems that tobacco use in our country is unchanging, while the trend in alcohol consumption is increasing. These findings and the decrease in new supraglottic cancer cases and the increase in glottic cancers cannot be explained with the studies mentioned, in which alcohol carcinogenesis is higher for the supraglottis than the glottis. It is possible that these epidemiological studies have been performed with issues that are not equivalent and the extrapolations we have applied in an attempt to remedy this may have led us to conclusions that are not truly representative. As mentioned in other publications, it is virtually impossible to investigate separately the epidemiology of the different anatomical parts of the larynx.[7]

In the light of all of this, we once again appeal to the accepted multifactorial theory of carcinogenesis. The factors and mechanisms of action that play a part in laryngeal cancer are currently unknown.

The change seen in favour of the glottic cancer sublocation is also not yet completely clear. Lifestyle changes in our country nowadays do not offer any explanation for this or for the continuing trend within our country.

We believe that other factors, such as improvements in diagnostic techniques and the trend towards classifying tumours as supraglottic when it is impossible to determine their origin, may have affected the classic trend of supraglottic tumour preponderance. Optical developments now used more and more in clinical practice have allowed us to fine-tune the diagnosis of laryngeal tumour locations. We must consider that there are tumours in advanced stages with glottosupraglottic (transglottic) disease in which it is neither clinically nor histopathologically possible to determine the true origin of the tumour. In the study by Maier et al[20] the percentage of cases in which there is no possibility of clearly differentiating supraglottic and glottic cancers is 34.1%.

It is believed that genetics and molecular or cell biology will in future allow us to acquire more knowledge about carcinogenesis in the larynx and the treatment and prevention of these tumours.

On the other hand, coinciding with other countries in which glottic tumours are predominant, it can be said that these are diagnosed in earlier stages than supraglottic ones.[17,18,21,22] In the series we studied, 83.1% of glottic carcinomas were diagnosed in early stages (T1 and T2), compared with 60.0% of supraglottic ones. If we only take into account the T1 category, the result is 73.46% of glottic carcinomas are diagnosed in the T1 stage versus 10.83% of supraglottic ones.

Nowadays, we can state that the incidence of glottic carcinomas in our setting is higher than that of supraglottic ones, showing an epidemiological change that we date from around 1985-1990 and has been maintained to date. This means the classic concept of Spain presenting a predominance of supraglottic tumours like most Mediterranean countries is no longer valid.

Most of these tumours are diagnosed early on, especially in stage T1, possibly linked to the early onset of the main presenting symptom, dysphonia, and the fact that the population is aware that a visit to the doctor is necessary if this symptom appears.

Recent lifestyle changes (tobacco, alcohol, and dietary habits) in our population do not explain this change nor the fact that the trend is stable, leading us to believe that there are other factors in play.

To sum up, we feel that long-term standardized epidemiological studies are necessary in order to analyze the same parameters and explain these changes in the future.

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