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Original Research Article

Factors involved in diagnosis delay and poor prognosis in laryngeal squamous carcinoma: a retrospective study about 86 cases

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ABSTRACT

Background: Squamous cell carcinoma of head and neck seems to be the seventh most common histological type worldwide with a great morbidity and mortality rates. Multiple published papers studied the overall survival of laryngeal squamous carcinoma depending on different factors. The aim of the study was to analyze the different factors that could impact the patient and the professional delays, and hence analyze factors related to poor prognosis and overall survival rates.
Methods: Retrospective descriptive and analytic study between January 2015 and January 2020 in ENT-HNS department in university hospital Mohammed VI of Marrakech. All patients admitted for confirmed histologically with a primary laryngeal squamous carcinoma and who consented to this study were included in our study, grouping 86 patients.
Results: Age and denial of care were the factors related to patient delay (p=0.044), medical doctors (0.030), the first consult decision (0.044) and the malpractice (0.008) were statistically related to the professional delay. The multivariate analysis with disease specific survival found that the tumor location (p=0.022), the disease staging at diagnosis (0.047), the Charlson comorbidity index (p=0.017), the patient delay and professional delay (p<0.001) were associated to a poor survival rate.
Conclusions: Patient and professional delays are factors that could be controlled by emphasizing the importance of medical consult when presenting laryngeal symptoms and the essential role of primary care doctors during 1st consult and how crucial it is to make a full examination and even refer patients to specialist when malignancy is suspected.

Keywords: Laryngeal squamous carcinoma, Delay in laryngeal carcinoma, Dysphonia

INTRODUCTION

Laryngeal cancer comes in the second place in all head and neck cancers and the squamous cell carcinoma of head and neck seems to be the seventh most common histological type worldwide.[1,2]

Nevertheless, this type of malignant tumors is often diagnosed in its advanced, aggressive stages, which leads to a great morbidity and mortality rates; as the clinical staging is directly related to a poor prognosis.[3-5]

This problematic has been the subject of multiple papers; studying the overall survival of laryngeal squamous carcinoma.[1-6] So, what are the incriminated factors leading to this delayed diagnosis and in consequence poor prognosis? What are the reasons behind patient and professional delay?

The objective of this study is to analyse the different factors that could impact the patient and the professional delays, and hence analyze factors related to poor prognosis and overall survival rates.

METHODS

We conducted a retrospective descriptive and analytic study between January 2015 and January 2020 in the ENT-HNS department in university hospital Mohammed VI of Marrakech.

We used a non-probability sampling method: Purposive sampling. The inclusion criteria were mainly based on a histologically confirmation of a primary laryngeal squamous carcinoma, to which no exclusion criteria were needed; we thus collected data from 86 patients.

Patient delay was defined by the time gap between the date of the constatation of the first symptom and the date of the first consult.

Professional delay was defined by the time gape between the date of the first consultation and the date of the diagnosis assessment.

Total delay was defined by the sum of both patient and professional delay. The delay is presented in weeks.

Charlson comorbidity index was used to categorize the patient status and we defined subgroups as follow: No comorbidity; CI score 0; Modest comorbidity; CI score 1-2; High comorbidity; CI score; 3 or more.

The statistical study was conducted using SPSS, all variable were categorized in groups.

We compared the groups using the Kruskal-Wallis tests.

The survival functions were determined using Kaplan-Meier method and compared using Breslow's test. The multivariate analysis used cox regression with disease-specific survival from the survival status at the time the study was conducted.

RESULTS

Epidemiological findings

Our studied population was mostly composed of male elderly as the mean age was 62.03 (45-86), with 95.3% males. Socioeconomical level was defined based on our country's social norms and 91.9% of our patients have a low socioeconomic level. We studied different variables that might be involved in the patient delay such as transportation cost and the distance to the nearest health facility and the most found reasons for patients delay were lack of means, denial of care and the use of traditional treatments.

Although all these factors can impact the extension of delays but the only two variables with a statistically significant difference found with the age (p=0.044) and the denial of care (p=0.042). Table 1 regroups the results of the statistical study. Figure 1 are plots of the statistical difference.

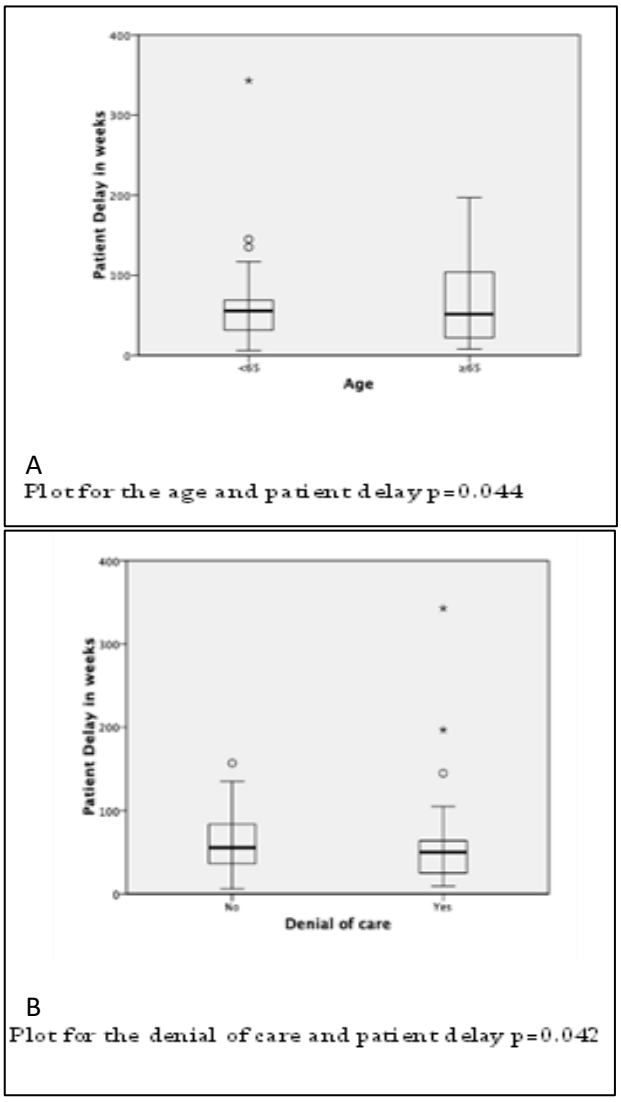

Figure 1 (A and B): Plot representation for age and denial of care per patient delay.

Patients' presentation

The 91.9% of our patients were smokers and drinkers. The comorbidity status evaluated by Charlson comorbidity index and categorized in subgroups found 69.8% of patients with modest comorbidity, 29.1% with high comorbidity and 1.2% with no comorbidity. General medical doctors' opinion was sought in 75.6% of cases, the 24.4% others went directly to a specialist. The major symptom found in patients was hoarseness in 95.3% other symptoms as pharyngalgia, neck lumps and dyspnea were less found in our series. The medical conduct was using medical treatment in 65.1%, to refer to a specialist in 11.6% cases and to undergo an endoscopic examination and a biopsy in 23.3% cases. There was a difference statistically significant with the professional delay and the medical doctor firstly consulted (p=0.030),

the medical conduct in the first consult (p=0.044) and the mismanagement (p=0.008). Table 2 regroups results of statistical study (Figure 2).

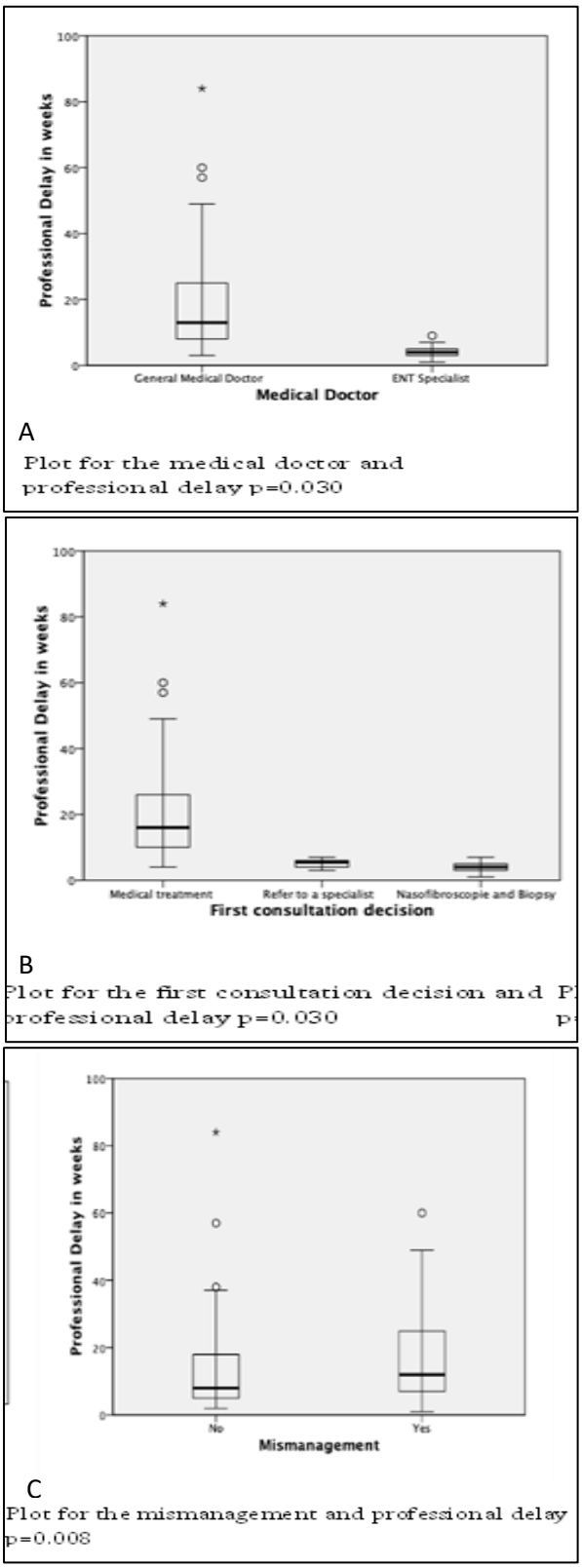

Figure 2 (A-C): Medical doctor, first consult decision and mismanagement denial of care per professional delay.

Diagnosis delay

The mean total delay in weeks was 76.36, with a minimum and maximum delay 9 and 373 weeks.

The mean patient and professional delay were respectively 61.49 (6-343) and 14.81 (1-84) weeks (Table 3).

The mean of patient delay was 61.49 weeks. and thought there was a difference between different groups of patients, the latest was not statistically significant. Same goes for the professional delay where the mean delay was 14.81 weeks.

Diagnosis delay and survival

The patients aged 65 or more, smokers and drinkers were not related to over-all survival as shown respectively in Figure 3.

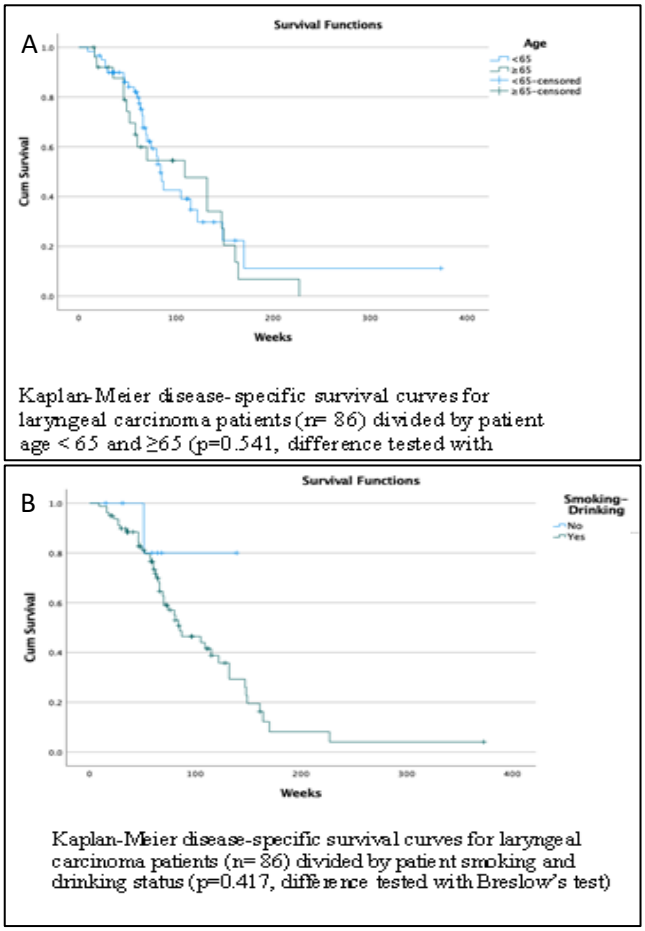

Figure 3 (A and B): Kaplan-Meier disease-specific survival curves for laryngeal carcinoma patients for age and smoking and drinking.

The comparison showed a meaningful statistical relationship between the number of comorbidity and the disease staging at diagnosis with the overall survival (Figure 4).

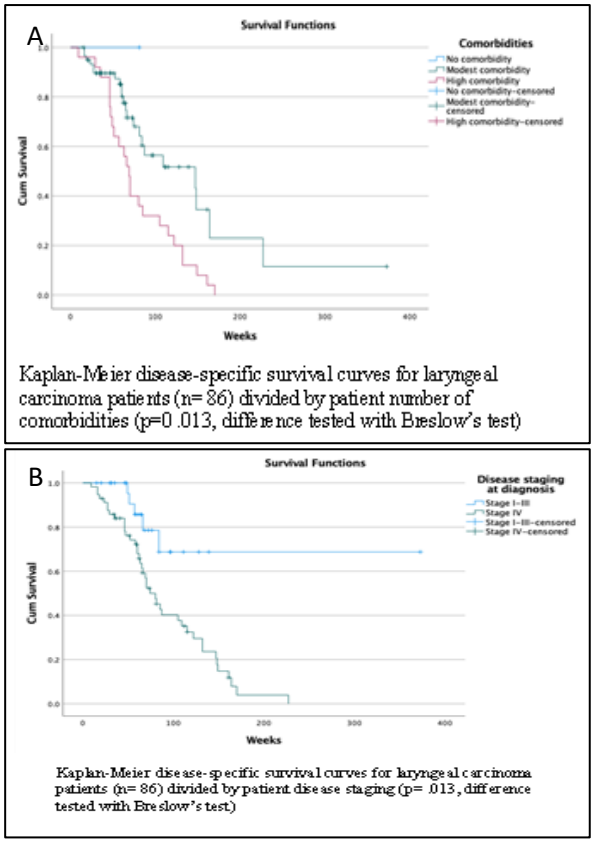

Figure 4 (A and B): Kaplan-Meier disease-specific survival curves for laryngeal carcinoma patients for comorbidities and disease staging at diagnosis.

The multivariate analysis showed that the glottic tumor location (p=0.022), the stage IV of the disease (p=0.047) the high comorbidity (p=0.017) and the patient and the professional delay (p<0.001) are strongly associated with poor prognosis and the overall survival. The cox regression analysis results are presented in Table 4 and the graphical presentation of the equation is presented in Figure 5.

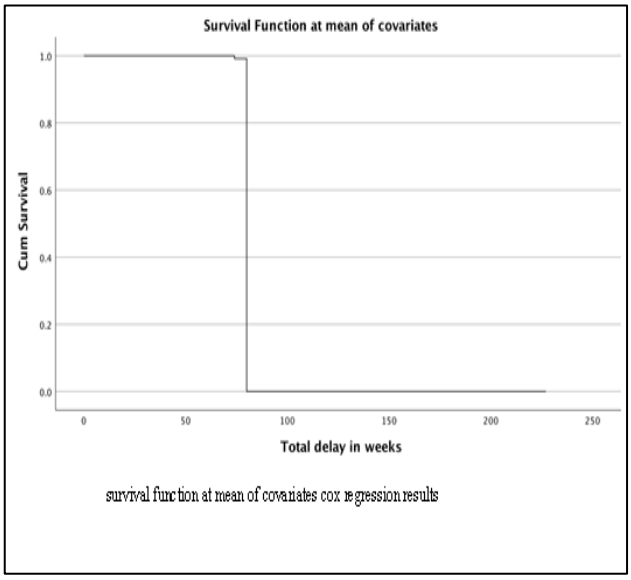

Figure 5: Cox regression graphical representation.

Table 1: Statistical results comparing different variables with patient delay intervals.

Variables	Patient delay	Mean rank	P value
Age (years)	<26	42.44	0.044*
	26-54	34.60	
	54-104	45.68	
	≥104	53.65	
Sex	<26	43.89	0.855
	26-54	43.55	
	54-104	44.03	
	≥104	41.50	
Comorbidities	<26	45.67	0.689
	26-54	40.17	
	54-104	42.75	
	≥104	47.85	
Origin	<26	39.39	0.552
	26-54	48.26	
	54-104	42.06	
	≥104	45.27	
Profession	<26	40.06	0.459
	26-54	45.86	
	54-104	41.88	
	≥104	48.69	
Socioeconomic level	<26	39.25	0.507
	26-54	40.67	
	54-104	45.25	
	≥104	49.38	

Continued.

Variables	Patient delay	Mean rank	P value
Academic level	<26	41.50	0.859
	26-54	42.38	
	54-104	43.29	
	≥104	48.62	
Social status	<26	43.03	0.934
	26-54	44.98	
	54-104	43.03	
	≥104	43.00	
Housing situation	<26	42.22	0.163
	26-54	47.00	
	54-104	40.68	
	≥104	47.00	
Distance to the nearest health care facility	<26	38.19	0.548
	26-54	40.88	
	54-104	47.13	
	≥104	45.58	
First symptom	<26	41.50	0.434
	26-54	45.62	
	54-104	44.01	
	≥104	41.50	
Lack of means	<26	49.28	0.600
	26-54	43.48	
	54-104	40.71	
	≥104	42.85	
Denial of care	<26	38.44	0.042*
	26-54	36.74	
	54-104	45.47	
	≥104	56.27	
Use of traditional treatment	<26	41.00	0.691
	26-54	39.98	
	54-104	46.06	
	≥104	45.96	

*Statically significant p<0.05.

Table 2: Statistical results comparing different variables with professional delay intervals.

Variables	Professional delay	Mean rank	P value
Mismanagement	<26	47.63	0.008*
	26-54	36.46	
	54-104	41.96	
	≥104	57.30	
Difficulty in diagnosis	<26	39.00	0.779
	26-54	43.96	
	54-104	43.65	
	≥104	44.73	
Medical doctor	<26	38.38	0.030*
	26-54	49.54	
	54-104	37.65	
	≥104	50.20	
First consultation decision	<26	34.50	0.044*
	26-54	48.92	
	54-104	38.15	
	≥104	52.10	
	Total		

*Statically significant p<0.05.

Table 3: Patient distribution as per different delays.

Delay intervals (weeks)	Patient delay (%)	Professional delay (%)	Total delay (%)
<26	18 (20.9)	8 (9.3)	8 (9.3)
26-54	21 (24.4)	26 (30.2)	22 (25.6)
54-104	34 (39.5)	37 (43.0)	36 (41.9)
≥104	13 (15.1)	15 (17.4)	20 (23.3)

Table 4: Results of the multivariate analysis using cox regression.

Variables	B	SE	Wald	df	Sig.	Exp (B)	95.0% CI for Exp (B)	
							Lower	Upper
Age (Years)	0.664	0.610	1.184	1	0.276	1.943	0.587	6.424
Smoking	-1.159	1.405	0.681	1	0.409	0.314	0.020	4.926
Tumor location	1.905	0.831	5.260	1	0.022*	6.719	1.319	34.227
Disease staging at diagnosis	1.688	0.848	3.960	1	0.047*	5.408	1.026	28.513
Patient delay in weeks	-2.248	0.629	12.759	1	<0.001*	0.106	0.031	0.363
Professional delay (weeks)	-2.251	0.633	12.633	1	<0.001*	0.105	0.030	0.364
Charlson comorbidity index	0.873	0.367	5.670	1	0.017*	2.394	1.167	4.910

*Statically significant p<0.05.

DISCUSSION

Squamous cell carcinoma of head and neck seems to be the seventh most common histological type worldwide with a great morbidity and mortality rates.[6] Laryngeal cancer as a subgroup account for 13360 cancer diagnosis and 3660 in the United States in 2017, This show the importance of the study of factors that may be impactful to reduce the mortality and also the quality of life in these patients, with an early diagnosis assessment and treatment start.[7]

Multiple published papers studied the overall survival of laryngeal squamous carcinoma depending on different factors. Our delays were much more extended, exceeding two years in some cases, than the ones reported in the literature this could be explained by difference of cultural and infrastructure difference between countries.[5-10]

Though there was no statistically significant relation between the patients socioeconomical level and the poor access to health care facilities in our study with patients delay, but Kompelli and al, and Ramos and al explained that population with poorer income and access to health care were associated with decreased hazard.[7,11]

The diagnosis of laryngeal tumor is in the end made by the consultant and chronic hoarseness is known to be the first symptom to make the practician suspect a laryngeal tumor and even malignancy, in the other hand patients tend to neglect it and this of it as a benign affection that's going to resolve spontaneously.[4,8,12] Conversely, when patients take their symptoms seriously and seek medical advice, their condition could be mislabelled.[8]

Schwartz and al published in 2009 clinical practice guideline for hoarseness and considered it an option to perform a laryngeal mirror examination or a laryngoscopy, reversing it smith and al find that the balance benefice risk tends to make it a recommendation or a strong recommendation to perform a laryngoscopy or refer for a laryngoscopy.[13,14]

In our case primary care doctors first choice was to treat patient they received for chronic dysphonia as a benign infection or as an acute laryngitis, instead of suspecting malignancy and referring the patient for a laryngoscopy. the first medical consultant and the first medical decision was highly associated with extended professional delays.

Daniel and al published on 2009 a paper on medical malpractice and cancer, they stated that 53% of their patients who accused hoarseness were not evaluated implying that when doctors should have performed a biopsy, they didn't, which led to patients thinking their laryngectomy was a consequence or a complication of the delay.[15]

This makes us think that doctors should be more sensitized about laryngeal cancers and the importance of the early diagnosis to prevent radical treatment that might affect the quality of life of patients, a mirrored laryngoscopy is a simple and unharmful examination that can make the practitioner suspect a laryngeal neoplasm, also referring to a laryngologist when not sure about the outcome of the examination is better than leaving the patient on medical treatment.[16,17]

In our multivariate analysis, multiple factors were identified as related to poor survival prognosis: tumor

location, the disease staging, comorbidity index and especially the patient and professional delays. In a study comparing pre-treatment delays between 1992 and 2002 it was found that the delays increased over the years.[9] Teppo and al conducted three different studies in 2003, 2008 and 2009, in the three papers the professional delay was strongly related to poor diagnosis, they also stated that the overall survival was related to patients delay, this also was found in smith and al study.[5,10,14,16] The comorbidity index impacting the overall survival in laryngeal cancers was studied by multiple authors and was found that patients with a high comorbidity index were unluckily to have a poor prognosis.[16,18-21]

The diagnosis staging was significantly related to poor diagnosis, as the sooner the diagnosis is mad the sooner the treatment is started and the higher the chances of survival are.[6,10,11,14,22]

Smoking and drinking as factors influencing the survival in laryngeal carcinoma, were studied but they had no statistically significant impact on the prognosis in our study neither in other studies, these results does't imply that patients with and without toxic consumption have the same disease progression .[10,11]

Seeing the results of all these studies, should make us think about ways, us laryngologists, can diminish the professional delay and raise awareness among younger health care givers on the importance of considering chronic dysphonia as a serious condition that could hide behind it a possible cancer diagnosis; make a full laryngeal examination in patients with risk factors who come into consultation, with or without laryngeal symptoms. And more importantly educate the general population, for them to understand the importance of seeking medical advice when presenting symptoms as hoarseness, dysphonia or even Pharyngalgial as it would reduce the patients and professional delays and thus the overall prognosis.[10,11,23]

Teppo and al stated in their paper that their sample size was small which may affect the generalizability of the results, this is the case for us too.[10] still the same results were found in larger samples making these findings of more importance.[24-26]

Nonetheless, these results must be interpreted with caution and a number of limitations should be borne in mind. A sampling and selection bias and a cultural bias should be considered, as patients don't always seek professional advice and rising awareness against chronic dysphonia and laryngeal carcinoma should help get a greater sample which would help in the generalization of the findings to the general population.

CONCLUSION

As shown by this study along with many others similar ones; patients and professional delays have a direct impact on the prognosis and overall survival in laryngeal carcinoma. We thus conclude our work with general recommendation aiming to the shortening of these delays; if a special interest is given to educating the general population on the importance of seeking medical advice when presenting chronic dysphonia, and raising awareness, regarding head and neck cancers in general and laryngeal cancer especially, among primary care givers to do laryngeal examination or refer to a specialist.

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