

Treatment of laryngeal cancer in a tertiary hospital - survival analysis of 10 years of experience

Original Article

Authors

Joana Barreto

Hospital Pedro Hispano, Matosinhos, Portugal

Pedro Marques Gomes

Hospital Pedro Hispano, Matosinhos, Portugal

Delfim Duarte

Hospital Pedro Hispano, Matosinhos, Portugal

Miguel Viana

Hospital Pedro Hispano, Matosinhos, Portugal

Abstract

Laryngeal cancer is the second most common neoplasm of the upper aero-digestive tract. The aim of this study is to epidemiologically characterize the patients with laryngeal cancer diagnosed and treated at our institution, as well as to carry out an analysis of their survival.

A retrospective study was conducted which included 150 patients with a mean age at diagnosis of 62.8 ± 9.5 years, 145 of whom were male, 92.5% had smoking habits and 83.7% had alcohol habits.

Patients with early stages at diagnosis (0, I and II) had a disease-related survival rate of 92% at 5 years compared to patients with advanced stages (III or IV), who had a survival rate of 58%.

As expected, patient survival varied significantly between all the different prognostic groups defined by the American Joint Committee on Cancer (AJCC) ($p < 0.001$).

Our study shows that patients with laryngeal carcinoma diagnosed and treated at our center have an epidemiology and survival rate comparable to those reported in the literature.

Keywords: Laryngeal Neoplasms; Survival Rate; Risk Factors; Prognosis.

Introduction

Laryngeal cancer ranks as the second most common upper aerodigestive tract neoplasm after oral cavity carcinoma¹. In Portugal, 529 new cases of laryngeal cancer were detected in 2020, with 329 deaths¹. It affects more men than women, with an overall ratio of 7:1¹.

The principal risk factors for this cancer are tobacco and alcohol use². Alone, each of these factors has a linear relationship with the risk of developing laryngeal cancer, but together, they have a synergistic effect². These risk factors are highly prevalent in the Portuguese population; however, there has been a decreasing trend in tobacco use since the 2000s, with 14% of Portuguese adults currently smoking tobacco

Correspondence:

Joana Barreto

joanaccabarreto@gmail.com

Article received on January 4, 2024.

Accepted for publication on April 3, 2024.

daily, which is below the 17% reported for the European Union (EU)³. Conversely, adult alcohol consumption is higher than the EU average^{3,4}, being 3.5-fold higher in men than in women⁴. The treatment depends on the disease stage⁵ at diagnosis. While surgery has traditionally been the primary approach for localized disease, non-surgical options such as radiotherapy and chemotherapy are viable options that can preserve organ function². The 5-year survival rate for patients with laryngeal carcinoma reportedly ranges between 54–56% in the United States⁶ and 58–65% in Denmark⁷. The objective of this study was to epidemiologically characterize the patients diagnosed and treated for laryngeal carcinoma in our institution, and to analyze their survival.

Materials and methods

A retrospective review was conducted of all cases of laryngeal carcinoma diagnosed and treated at our institution between January 1, 2013 and December 31, 2022. All patients diagnosed during this period were included in the study, with no selection criteria.

The parameters analyzed were age, sex, smoking habit, drinking habit, tumor site, histological type, disease stage at diagnosis according to the American Joint Commission on Cancer (AJCC)⁵, and type of treatment. We also examined the time between first otorhinolaryngologic observation and histological diagnosis, and in surgical cases, the time from surgical decision to the procedure. The descriptive analysis of continuous variables used mean and standard deviation (SD), and median and interquartile range (IQR) for variables with a non-normal distribution. Normal distribution was evaluated using the asymmetry and peakedness tests. Categorical parameters are presented as frequencies and percentages. Survival was analyzed by 5-year cumulative occurrence and the Kaplan-Meier method. Cox regression was used to analyze each of the variables separately to analyze their association with survival. Subsequently, statistically significant variables ($p < 0.05$) were

included in a multivariate analysis to exclude potential confounding factors.

Results

This study analyzed 150 patients diagnosed and treated for laryngeal carcinoma in the study period. The median time until diagnosis was 2.8 years, with an IQR of 3.9 years. The mean age at diagnosis was 62.8 ± 9.5 years and the study included 145 (96.7%) men and five women. Regarding risk factors, 92.5% participants had a smoking habit; 19.4% were ex-smokers and 73.1% active smokers at diagnosis. Only 7.5% of the patients had never smoked, and 83.7% of the study sample reported drinking alcohol.

The most common tumor site was the glottis (70.7%), followed by the supraglottis (28.0%) and subglottis (1.3%). Most of the patients (58%) had advanced (stage III or IV) laryngeal cancer at diagnosis. Additionally, patients with other synchronous or metachronous primary neoplasms were also identified, totaling 22 patients (14.7%) and 24 neoplasms, mostly lung cancer. Table 1 summarizes the patient data. Regarding treatment, 80% of the patients underwent surgery, which included transoral laser microsurgery (TLM) or total laryngectomy, with or without lymph node dissection, depending on the indication.

Survival is presented as overall survival (OS) and disease-specific survival (DS) in Table 2. Patients diagnosed with early stage (0, I, or II) laryngeal cancer had a 5-year DS of 92%, while those with advanced stage (III or IV) reached 58%. Considering all stages, the study sample demonstrated a 5-year OS of 65% and DS of 72%. Moreover, the most frequent cause of death not related to laryngeal carcinoma was lung cancer. Figure 1 displays the Kaplan-Meier curves for DS categorized by prognostic staging. As anticipated, patient survival exhibited significant variation among the different prognostic groups, with $p < 0.001$ in the logrank test. Figure 2 illustrates the Kaplan-Meier curves for DS categorized by the type of treatment, which was strongly influenced by the disease stage. Cox regression was employed to investigate the potential

Table 1		
	Patients (n=150)	
Age (years) - mean and SD	62,8 ± 9,5	
Sex - n (%)		
Male	145	(96,7)
Female	5	(3,3)
Time until diagnosis (years) - median and IQR	2,8	(2,9)
Time until diagnosis (days) - median and IQR	21	(14)
Time until surgery (days) - mean and SD	10,4 ± 8,1	
Smoking habit - n (%)		
Non-smoker	10	(7,5)
Ex-smoker	26	(19,4)
Smoker at diagnosis, but quit	74	(55,2)
Smoker at diagnosis and maintained	24	(17,9)
Drinking habit - n (%)	72	(83,7)
Histological type - n (%)		
Squamous cell carcinoma	146	(97,3)
Sarcomatoid variant	3	(2,0)
Warty variant	1	(0,7)
Staging - T - n (%)		
Tis	3	(2,0)
T1	35	(23,3)
T2	31	(20,7)
T3	47	(31,3)
T4a	32	(21,3)
T4b	2	(1,3)
Staging - N - n (%)		
N0	103	(69,1)
N1	8	(5,4)
N2a	6	(4,0)
N2b	9	(6,0)
N2c	12	(8,1)
N3a	3	(2,0)
N3b	8	(5,4)
Staging - M - n (%)		
M0	142	(95,9)
M1	6	(4,1)
Prognostic staging - n (%)		
0	3	(2,0)
I	35	(23,6)
II	24	(16,2)
III	31	(20,9)
IVa	37	(25,0)
IVb	12	(8,1)
IVc	6	(4,1)
Site - n (%)		
Supraglottic	42	(28,0)
Glottic	106	(70,7)
Subglottic	2	(1,3)
Main treatment - (%)		
TLM	61	(40,7)
Total laryngectomy	60	(40,0)
CRT	15	(10,0)
RT	4	(2,7)
Palliative treatment	10	(6,7)
Postoperative adjuvant therapy - n (%)		
Not applicable	29	(19,3)
None	64	(42,7)
RT	37	(24,7)
CRT	20	(13,3)
Synchronous or metachronous neoplasms - n (%)	22	(14,7)

Note: IQR - Interquartile Range; SD - Standard Deviation; TLM - Transoral Laser Microsurgery; CRT - Chemoradiotherapy; RT - Radiotherapy. *9 missing values for smoking habits; 64 missing values for drinking habits; 1 missing value for staging - N; 2 missing values for staging - M; 2 missing values for prognostic staging.

Table 2

Prognostic staging	n (%)	Disease-specific survival		Overall survival	
		1 year	5 years	1 year	5 years
0	3 (2%)	100%	100%	100%	100%
I	35 (23,6%)	100%	95%	100%	91%
II	24 (16,2%)	95%	87%	87%	61%
III	31 (20,9%)	97%	73%	97%	70%
IVa	37 (25,0%)	92%	61%	92%	53%
IVb	12 (8,1%)	58%	38%	58%	38%
IVc	6 (4,1%)	64%	0%	64%	0%
All	150 (100%)	92%	72%	90%	65%

associations between survival and variables of age, sex, smoking habit, drinking habit, tumor site, and histological type, and showed no significant associations.

Nevertheless, both the AJCC prognostic stage and type of treatment showed a statistically significant association with survival when analyzed individually. After adjustment for confounding factors via multivariate analysis, while the type of treatment showed a non-

significant association, the prognostic stage retained its significant value. Cox regression revealed a hazard ratio of 9.1 for advanced stages (III or IV) over early stages (0, I or II), with $p < 0.001$. Patients with advanced tumors were further examined separately to compare survival between those undergoing surgical (total laryngectomy) and those receiving systemic treatment with chemoradiotherapy (CRT). After adjustment for the confounding

Figure 1

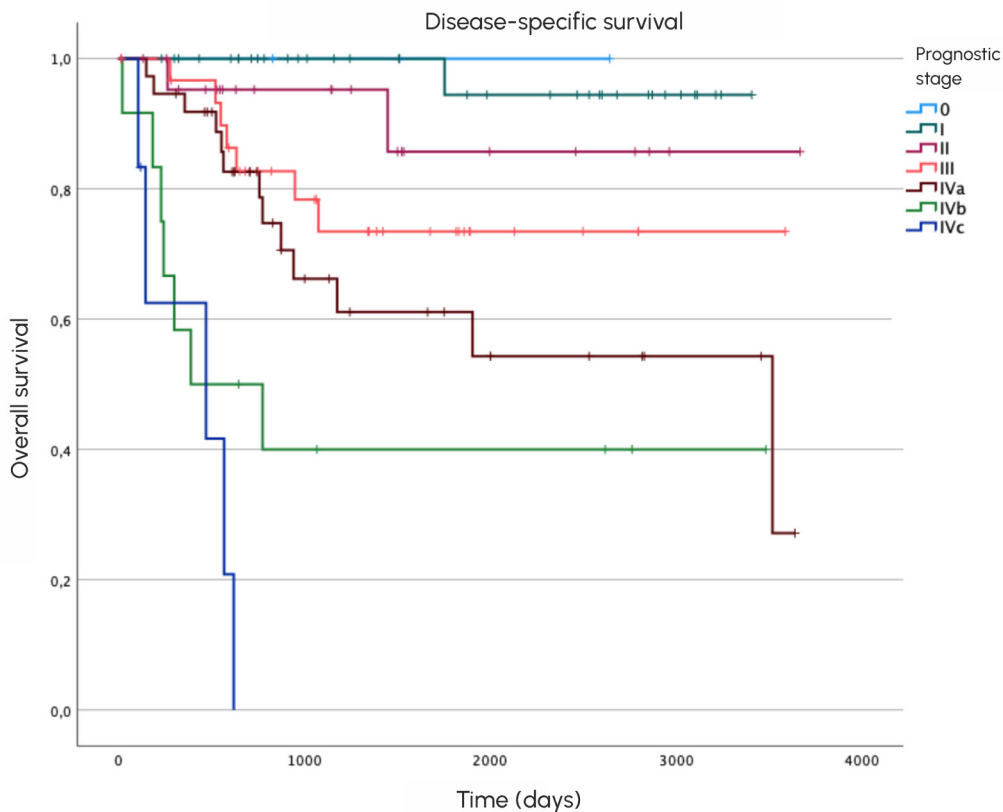
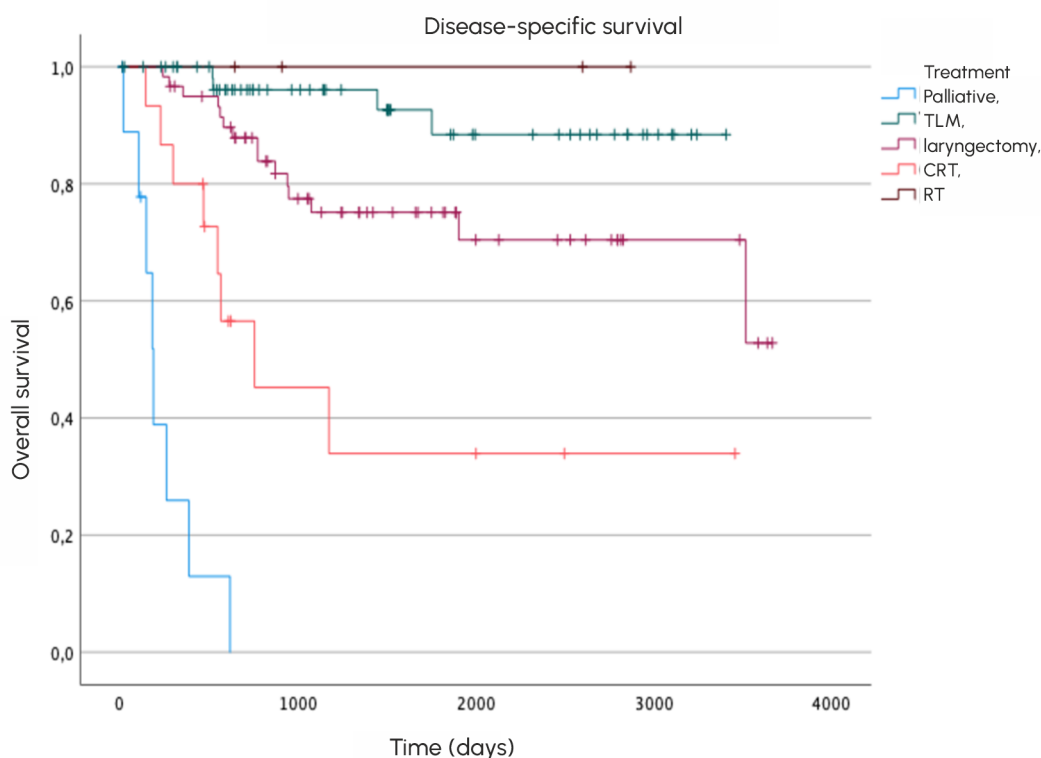


Figure 2



factor of prognostic stage, there was no statistically significant differences in survival between the surgical and systemic treatments groups ($p = 0.08$).

Discussion

This study presents the results of 150 cases of laryngeal cancer diagnosed and treated at our institution. The proportion of male to female patients (29:1) was much higher than that described in the literature¹, possibly due to the higher prevalence of risk factors in men. Most patients seeking otorhinolaryngologic treatment had advanced stage cancer, corresponding to 58% of the cases. Regarding the treatment used, most patients (121) underwent surgery. Among the surgical modalities used, patients undergoing TLM had a higher survival rate than the ones undergoing total laryngectomy, possibly reflecting the observed staging differences, since tumors resected by TLM are smaller and more localized. Although some studies have reported similar survival between surgical and systemic treatments for locally advanced

tumors⁸, others showed better survival with surgery⁹⁻¹¹. Overall, there is a preference for surgery in our institution, with only 15 cases referred for radical CRT, comprising patients refusing surgery, not eligible for anesthesia or surgery, or with tumors including unresectable structures. Figure 2 shows that the patients undergoing this treatment had a lower survival curve than patients undergoing surgery. However, there was a selection bias in patients referred for CRT, with no statistically significant survival differences found between patients with advanced tumors undergoing surgery and those receiving CRT after adjustment for confounding factors. The group with the AJCC prognostic stage II had a much lower OS than DS, as this group had more deaths from other causes (lung cancer). There was no statistically significant associations between survival and variables of age, sex, smoking habit, drinking habit, tumor site, and histological type. Nevertheless, the AJCC prognostic stage and treatment type individually exhibited a statistically significant association with survival. In multivariate analysis, the type

of treatment showed a non-significant association with survival, but prognostic stage retained a significant association. This shows that the type of treatment is closely related with disease staging, which impacts survival, being a confounding factor. Cox regression analysis showed a hazard ratio of 9.1 for advanced stages (III or IV) over early stages (0, I or II), with $p < 0.001$. This means that patients with advanced stage cancer have a mortality rate which is 9.1-fold higher than that of patients with early stage cancer. This fact, combined with the observation that most patients seek an otorhinolaryngological consultation at advanced stages, shows the importance of raising awareness about laryngeal cancer for ensuring an early diagnosis, especially in smokers. The 5-year DS and OS rates of all patients in our center were 72% and 65%, respectively, which are similar or even superior to the survival rates for laryngeal carcinoma reported in other studies^{6, 7, 12}. We also emphasize that the time from first appointment to histological diagnosis of laryngeal carcinoma in our center is less than a month, with a median of 21 days, considering that most cases require general anesthesia to obtain the tumor sample, and that, in case of surgical patients, the mean waiting time for surgery is just 10 days (Table 1). In summary, many of our patients wait less than a month for surgical treatment after the first appointment, and early treatment is one of the most important prognostic factors for these patients. However, as this is a retrospective study, some missing data due to partial clinical records may have affected our results.

Conclusion

Our patient cohort exhibited a high prevalence of risk factors such as alcohol consumption and smoking habits, with many seeking treatment at a relatively advanced stage of laryngeal cancer. This study shows that patients with laryngeal carcinoma diagnosed and treated in our institution have a good DS, as they are quickly diagnosed and treated.

Conflicts of Interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

Data Confidentiality

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

Protection of humans and animals

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the 2013 Helsinki Declaration of the World Medical Association.

Funding Sources

This work did not receive any contribution, funding or scholarship.

Availability of scientific data

There are no datasets available, publicly related to this work.

Bibliographic references

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A. et al. Global Cancer Statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2021 May;71(3):209-249. doi: 10.3322/caac.21660.
2. Steuer CE, El-Deiry M, Parks JR, Higgins KA, Saba NF. An update on larynx cancer. *CA Cancer J Clin.* 2017 Jan;67(1):31-50. doi: 10.3322/caac.21386.
3. OCDE/Observatório Europeu dos Sistemas e Políticas de Saúde (2021), Portugal: Perfil de Saúde do País 2021, Estado da Saúde na UE, OCDE, Paris/Observatório Europeu dos Sistemas e Políticas de Saúde, Bruxelas. Disponível em: https://health.ec.europa.eu/system/files/2021-12/2021_chp_pt_portuguese.pdf
4. Serviço de Intervenção nos Comportamentos Aditivos e nas Dependências (SICAD), Direção de Serviços de Monitorização e Informação (DMI) DodEselaoD. SINOPSE ESTATÍSTICA 2021 – Álcool.
5. Amin MB, Edge S, Greene F, Byrd DR, Brookland RK, Washington MK, et al. *AJCC Cancer Staging Manual*. 8th ed. Springer International Publishing: American Joint Commission on Cancer. 2017.
6. Li MM, Zhao S, Eskander A, Rygalski C, Brock G, Parikh AS. et al. Stage migration and survival trends in laryngeal cancer. *Ann Surg Oncol.* 2021 Nov;28(12):7300-7309. doi: 10.1245/s10434-021-10318-1.
7. Nahavandipour A, Jakobsen KK, Gronhoj C, Hebbelstrup Jensen D, Kim Schmidt Karnov K, Klitmoller Agander T. et al. Incidence and survival of laryngeal cancer in Denmark:

- a nation-wide study from 1980 to 2014. *Acta Oncol.* 2019 Jul;58(7):977-982. doi:10.1080/0284186X.2019.1572923.
8. Timme DW, Jonnalagadda S, Patel R, Rao K, Robbins KT. Treatment selection for T3/T4a laryngeal cancer: chemoradiation versus primary surgery. *Ann Otol Rhinol Laryngol.* 2015 Nov;124(11):845-51. doi:10.1177/0003489415588130.
9. Kohler HF, Carvalho GB, Kowalski LP. Treatment results for stage III laryngeal cancer: analysis of a populational database using propensity scores. *Int Arch Otorhinolaryngol.* 2021 Nov 3;26(3):e370-e379. doi:10.1055/s-0041-1726042.
10. Arboleda LPA, Neves AB, Kohler HF, Vartanian JG, Candelária LM, Borges MF. et al. Overview of glottic laryngeal cancer treatment recommendation changes in the NCCN guidelines from 2011 to 2022. *Cancer Rep (Hoboken).* 2023 Aug;6(8):e1837. doi:10.1002/cnr2.1837.
11. Stokes WA, Jones BL, Bhatia S, Oweida AJ, Bowles DW, Raben D. et al. A comparison of overall survival for patients with T4 larynx cancer treated with surgical versus organ-preservation approaches: a national cancer data base analysis. *Cancer.* 2017 Feb 15;123(4):600-608. doi:10.1002/cncr.30382.
12. da Cunha Costa TF, Cardoso E. Carcinoma da laringe – 7 anos de experiência num hospital central. *Port J ORL [Internet].* 2017 Oct 30 [cited 2023 Dec 5];54(4):255-9. Available from: <https://sporl.josekarvalho.net/index.php/sporl/article/view/657>