Laryngeal Cancer in Young Patients: A Retrospective Study at Hassan II University Hospital, Fez

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2 3 **Abstract** 4 5 6 Background: Laryngeal cancer typically affects older individuals, most commonly between 50 7 and 70 years, often linked to tobacco and alcohol exposure. It remains rare in young adults under 40 years, and its clinicopathological characteristics and treatment outcomes are less 8 9 well defined. 10 **Objective:** To describe the epidemiological, histological, therapeutic, and evolutionary features of laryngeal cancer in young patients treated at Hassan II University Hospital, Fez. 11 Methods: A retrospective descriptive study was conducted from January 2012 to December 12 2024. Inclusion criteria were patients ≤40 years, histologically confirmed laryngeal cancer, 13 14 and complete clinical records. 15 **Results:** Among 272 patients, 6 (2.2%) were ≤40 years (mean age 34.3, 66.7% male). Two patients (33.3%) reported smoking, while none consumed alcohol. Most tumors were glottic 16 17 (83.3%), ulceroproliferative (50%), and squamous cell carcinoma (100%), with T3 and T4 18 equally distributed. Laryngeal preservation by chemoradiotherapy was achieved in 50%, while two patients underwent total laryngectomy followed by adjuvant radiotherapy. At a 19 mean follow-up of 8.5 years, 50% achieved complete remission and 50% experienced 20 21 recurrence (mean 68.3 months). **Conclusion:** Laryngeal cancer in young patients is rare. Despite lower exposure to traditional 22 risk factors, clinical, histological, and therapeutic characteristics mirror those of older 23 24 patients. 25 **Keywords:** Laryngeal cancer, young adults, squamous cell carcinoma, radiotherapy, 26 chemoradiotherapy 27 28 29 30 31

34 35 36 Introduction 37 Laryngeal carcinoma is among the most frequent head and neck malignancies and is 38 39 classically linked to tobacco and alcohol exposure, with peak incidence between 50 and 70 40 years [1,2]. In contrast, young adults (\leq 40 years) constitute a small fraction (\approx 2–5%) of cases 41 [3,4], a pattern recognized since early reports in the 1980s [5]. Whether younger patients 42 present with more advanced disease or experience distinct outcomes remains debated, with 43 contemporary series showing mixed results [6,7]. Current management emphasizes organ 44 preservation when oncologically safe, alongside a continued role for surgery in advanced or refractory disease [8–11]. For clinical background and therapeutic principles used in practice, 45 we also refer to the EMC chapter on laryngeal cancers [12]. 46 47 The aim of this study was to characterize the epidemiological profile, histopathological findings, therapeutic approaches, and treatment outcomes of laryngeal cancer in patients 48 ≤40 years old treated atHassan II University Hospital, Fez. 49 **Materials and Methods** 50 51 This was a retrospective descriptive study performed at the Department of Radiotherapy and Brachytherapy, CHU Hassan II, Fez, covering a 13-year period from January 2012 to 52 December 2024. 53 54 **Inclusion criteria** Age ≤40 years 55 Histologically confirmed laryngeal carcinoma 56 57 Received treatment at Hassan II University Hospital Complete and analyzable medical records 58 Data collection 59 Variables included: demographic data, risk factors, tumor site, macroscopic and histological 60 features, TNM stage, treatment modalities, and outcomes (remission, recurrence, survival). 61 62 Follow-up duration was recorded from the end of treatment to the last consultation. 63 **Analysis** 64 Descriptive statistics were applied. Categorical data were expressed as frequencies and 65 percentages; continuous variables as means and ranges. 66

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Results

Among 272 patients diagnosed with laryngeal carcinoma, 6 (2.2%) were aged ≤40 years. The mean age was 34.3 years, with a male-to-female ratio of 2:1. None of the patients reported a family history of cancer. Tobacco exposure was present in two patients (33.3%), while none reported alcohol consumption.

The primary tumor site was predominantly glottic (5/6 patients, 83.3%), with one supraglottic case (16.7%). This distribution is shown in **Figure 1**.

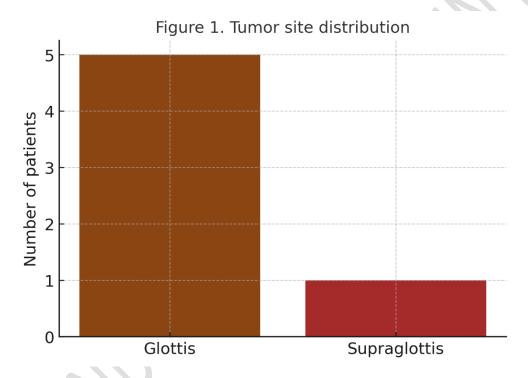


Figure 1. Tumor site distribution

Histopathologically, all tumors were squamous cell carcinomas, with well-differentiated histology in two cases (33.3%). Half of the patients were staged T3 and the other half T4, with nodal involvement in one case (16.7%). Macroscopically, half of the tumors exhibited an ulceroproliferative pattern.

Regarding treatment, three patients (50%) underwent organ-preserving concurrent chemoradiotherapy, one patient (16.7%) received radiotherapy alone, and two patients (33.3%) underwent total laryngectomy with bilateral neck dissection followed by adjuvant radiotherapy. The distribution of treatment modalities is illustrated in **Figure 2**.

Figure 2. Treatment modalities

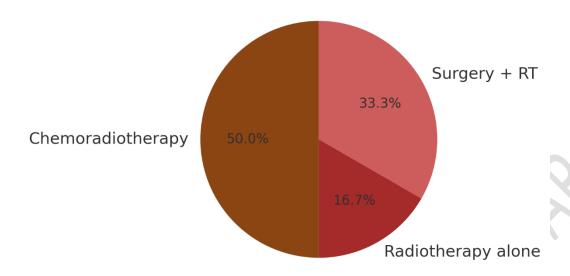


Figure 2. Treatment modalities

Both surgical cases had negative margins, no perineural invasion, and no vascular emboli. The mean interval between surgery and adjuvant radiotherapy was three months.

After a mean follow-up of 8.5 years (range: 4–13 years), three patients (50%) achieved complete remission, while three patients (50%) experienced recurrence, with a mean recurrence interval of 68.3 months (range: 12–136 months). Recurrence-free survival is depicted in **Figure 3**.

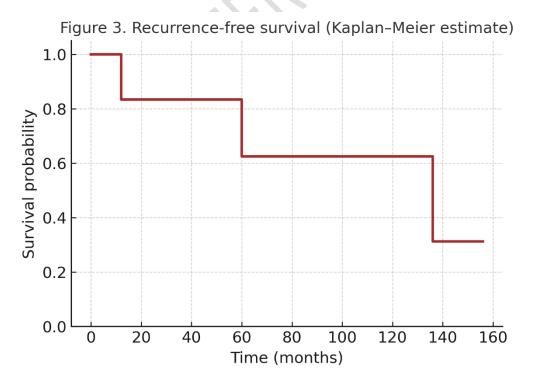


Figure 3. Recurrence-free survival (Kaplan-Meier estimate)

- 99 No patient developed a second primary tumor during follow-up.
- 100 **Discussion**
- 101 Rarity and epidemiology. Young adults represented 2.2% of our laryngeal cancer population,
- in line with reported ranges of **2–5%** across series and reviews [3,4]. Classic epidemiologic
- overviews also reaffirm the overall burden in older adults and the central role of lifestyle
- 104 exposures [1].
- 105 **Risk profile.** Only one-third of our young patients smoked and none reported alcohol use,
- echoing findings that classical risk factors may be **less prevalent** in younger cohorts [3,4,6].
- Nonetheless, the synergistic carcinogenic effect of tobacco and alcohol is well established
- and likely shapes outcomes in older populations [2].
- 109 Clinicopathologic pattern. The glottic predominance (83.3%) mirrors prior observations in
- young patients [3,4,6]. Histology showed conventional squamous cell carcinoma without
- distinctive features versus older cohorts, as also noted in historical and modern series [5–7].
- 112 **Treatment and organ preservation.** Our real-world management—**chemoradiotherapy** for
- laryngeal preservation when feasible and total laryngectomy for advanced or unsuitable
- cases—aligns with landmark organ-preservation trials and subsequent practice analyses [8–
- 115 11]. These data caution against over-generalizing randomized trial results to all patients,
- emphasizing individualized decision-making [10]. Comprehensive clinical references such as
- 117 **EMC** continue to support pragmatic management choices in daily practice [12].
- 118 **HPV and alternative etiologies.** Given the attenuated exposure to classical carcinogens
- among young patients, HPV-related oncogenesis warrants consideration. Meta-analyses and
- focused reviews suggest an association between HPV infection and laryngeal cancer, though
- the magnitude and clinical implications are still being refined [13,14]. Future work should
- integrate virologic testing and molecular profiling to clarify pathogenesis and guide therapy
- in this subgroup.
- 124 Limitations. Small sample size, retrospective design, and potential under-reporting of
- exposures limit inference. Nevertheless, the long follow-up adds value to outcome estimates.
- 126 Implications. Despite lower exposure to traditional risks, young-adult disease resembles that
- in older patients regarding site, histology, stage, treatment, and recurrence. Vigilant
- surveillance and multidisciplinary care remain essential.
- 129 Conclusion
- Laryngeal carcinoma in young adults is rare, accounting for only 2.2% of cases in our
- institution. Despite reduced exposure to conventional risk factors, the disease behaves
- similarly to that in older patients in terms of stage at presentation, histopathology, and
- prognosis. Early detection, organ-preserving strategies, and vigilant follow-up remain crucial.
- 134 Future research should focus on molecular and viral factors, particularly HPV, to better
- understand the etiology in this population.

Ethics Statement

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- 138 This retrospective study was conducted in accordance with the ethical standards of the
- institutional research committee and with the principles of the Declaration of Helsinki (1964)
- and its later amendments. Given the retrospective nature of the analysis and the
- anonymization of patient data, formal ethical approval and individual patient consent were
- waived by Hassan II University Hospital.

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Conflict of Interest

148 The authors declare that they have no conflict of interest.

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References

- 1. Hoffman HT, et al. Epidemiology of laryngeal cancer. *Otolaryngol Clin North Am.* 2008;41(4):761–769. doi:10.1016/j.otc.2008.01.001.
- Hashibe M, Brennan P, Chuang SC, et al. Interaction between tobacco and alcohol use and the risk of head and neck cancer: pooled analysis in the International Head and Neck Cancer Epidemiology Consortium. *Cancer Epidemiol Biomarkers* Prev. 2009;18(2):541–550. doi:10.1158/1055-9965.EPI-08-0347.
- Lechien JR, Fakhry N, Zelenik K, et al. Epidemiological, clinical and oncological outcomes of young patients with laryngeal cancer: a systematic review. *Eur Arch Otorhinolaryngol*. 2022;279(12):5635–5652. doi:10.1007/s00405-022-07466-9.
- Nachalon Y, Cohen O, Alkan U, Shvero J, Popovtzer A. Characteristics and outcome of laryngeal squamous cell carcinoma in young adults. *Oncol Lett*.2017;13(3):1393–1397. doi:10.3892/ol.2016.5528.
- 5. Shvero J, Hadar T, Segal K, Abraham A, Sidi J. Laryngeal carcinoma in patients 40 years of age and younger. *Cancer*.1987;60(12):3092–3095. doi:10.1002/1097-0142(19871215)60:12<3092::AID-CNCR2820601239>3.0.CO;2-H.
- Yang A, Tanamal P, Tibbetts K, et al. Characteristics and outcomes of young patients
 with laryngeal cancer: national hospital-based retrospective cohort analysis. *Head Neck*.2022 ;44(10):2095–2108. doi:10.1002/hed.27120.
- Li R, Yu S, Zhu W, Wang S, Yan L. Studying the impact of young age on prognosis and treatment in laryngeal squamous cell carcinomas using the SEER database.
 PeerJ.2019;7:e7368. doi:10.7717/peerj.7368.

- 8. Forastiere AA, Goepfert H, Maor M, et al. Concurrent chemotherapy and radiotherapy for organ preservation in advanced laryngeal cancer. *N Engl J Med*.2003;349(22):2091–2098. doi:10.1056/NEJMoa031317.
- 9. Forastiere AA, Zhang Q, Weber RS, et al. Long-term results of RTOG 91-11: three nonsurgical strategies to preserve the larynx. *J Clin Oncol*.2013;31(7):845–852. doi:10.1200/JCO.2012.43.6097.
- 10. Sanabria A, Chaves ALF, Kowalski LP, et al. Organ preservation with chemoradiation in advanced laryngeal cancer: generalizing results from randomized controlled trials.
 Auris Nasus Larynx. 2017;44(1):18–25. doi: 10.1016/j.anl.2016.06.005.
- 11. Bozec A, Culié D, Poissonnet G, Dassonville O. Current role of total laryngectomy in the era of organ preservation. *Cancers (Basel)*.2020;12(3):584. doi :10.3390/cancers12030584.
- 12. Prades JM, Reyt E. Cancers du larynx. *EMC Oto-rhino-laryngologie*.2013;8(4):1–20. doi:10.1016/S0246-0351(13)58510-2.
- 13. Li X, Gao L, Li H, et al. Human papillomavirus infection and laryngeal cancer risk: a systematic review and meta-analysis. *J Infect Dis*. 2013;207(3):479–488. doi:10.1093/infdis/jis698.
- 14. Torrente MC, Rodrigo JP, Haigentz M Jr, et al. Human papillomavirus infections in laryngeal cancer. *Head Neck*.2011;33(4):581–586. doi:10.1002/hed.21421.

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