European Archives of Oto-Rhino-Laryngology
https://doi.org/10.1007/s00405-021-06651-6

HEAD AND NECK

Open partial horizontal laryngectomy and adjuvant (chemo) radiotherapy for laryngeal squamous cell carcinoma: results from a multicenter Italian experience

Luca Muscatello[1] · Cesare Piazza[2,3] · Giorgio Peretti[4] · Filippo Marchi[4] · Andy Bertolin[5] · Erika Crosetti[6] · Gianluca Leopardi[7] · Riccardo Lenzi[8] · Laura Manca[9,10] · Jacopo Matteucci[8] · Raul Pellini[11] · Gerardo Petruzzi[11] · Livio Presutti[12] · Antonio Sarno[13] · Giovanni Succo[6] · Sara Valerini[12] · Giuseppe Rizzotto[5]

Received: 10 December 2020 / Accepted: 27 January 2021

Abstract

Purpose To evaluate the functional and oncologic outcomes of adjuvant (chemo)radiation [(C)RT] after open partial horizontal laryngectomies (OPHLs).

Methods Multicenter retrospective evaluation of 130 patients (116 males, 14 females) submitted between 1995 and 2017 to OPHL Types II and III for laryngeal cancer and receiving adjuvant (C)RT for one or more of the following risk factors at histopathologic examination of the surgical specimen: pT4a and/or > pN2a categories, close/positive resection margins, or presence of both perineural (PNI) and lympho-vascular invasion (LVI). The primary study endpoints were evaluation of the presence of tracheostomy and/or gastrostomy at last follow-up, and calculation of laryngo-esophageal dysfunction-free survival (LEDFS).

Results Mean age of the study cohort was 60.8 ± 8.9 years (median, 62; interquartile range [IQR], 13). Mean follow-up was 50.7 ± 39.4 months (range 24–188; median, 38; IQR, 51). Adjuvant therapy consisted of CRT in 53 (41%) patients, and RT alone in 77 (59%). Five-year LEDFS was 85%. Overall survival was 71.5%, while 13% of patients remained tracheostomy- and 3% gastrostomy-dependent at the last follow-up. The only significant variable in predicting survival ($p = 0.020$) was tracheostomy dependence: it was maintained in 7.5% of subjects after OPHL Type II and in 34% of those submitted to OHPL Type III ($p < 0.001$).

Conclusions In selected patients affected by advanced laryngeal cancer, OPHLs Type II and III have a relatively good laryngeal safety profile and provide favorable oncologic outcomes even in case of need for adjuvant (C)RT.

Keywords Head and neck cancer · Laryngeal cancer · Laryngectomy · Adjuvant radiotherapy · Adjuvant chemotherapy · Concomitant chemoradiotherapy · Speech · Deglutition · Radiation effects

Introduction

Advanced laryngeal cancers (LC) are a heterogeneous subset of lesions differing greatly in terms of biologic behaviors, patterns of diffusion, location, and possible host comorbidity profile. These intrinsic differences have been traditionally regarded as the most important source of difficulty in accurately delineating clear-cut and reproducible guidelines for treatment of LC, especially if one considers not only oncologic outcomes, but also functional and organ preservation issues. In line with this assumption, the latest American Society of Clinical Oncology (ASCO) position paper states that "for patients with locally advanced (T3, T4a) disease, organ-preservation surgery, combined chemotherapy and radiation, or radiation alone offer the potential for larynx preservation without compromising overall survival". However, recommendation 2.2 points out that "for selected patients with extensive T3 or large T4a lesions and/or poor pre-treatment laryngeal function, better survival rates and quality of life may be achieved with total laryngectomy (TL) rather than with organ-preservation approaches and may be the preferred approach" [1]. Thus, after decades of organ-preservation strategies and endless debates between surgical

✉ Riccardo Lenzi
riclenzi@gmail.com

Extended author information available on the last page of the article

Published online: 18 February 2021

and non-surgical enthusiasts, we are still far from having proper selection criteria.

In such a multifaceted scenario, the role of partial laryngectomies, in spite of their long history and well-known oncologic soundness, has shown fluctuating results with unequal geographical distribution, in both Europe and the Americas. The wide variety of operations described and recent widespread diffusion of alternative therapeutic options (transoral laser microsurgery [TLM] on one hand and chemoradiation [CRT] on the other) have further complicated this issue. Nowadays, the most frequently used techniques for open partial horizontal laryngectomy (OPHL) are supracricoid laryngectomies, described back in the 1970s mostly by French authors [2–4] and, more recently, by supratracheal techniques, described mainly by Italian surgeons [5]. In 2014, the European Laryngological Society (ELS), confirming the diffusely perceived need for an easy classification tool, introduced a comprehensive nomenclature system of OPHLs as Type I (supraglottic), Type II (supracricoid), and Type III (supratracheal), with conservation (a) or sacrifice (b) of the epiglottis and/or resection of one arytenoid (+ ary) [6].

This has greatly helped in having a much clearer picture of the possible oncologic and functional outcomes obtainable by different types of OPHLs in carefully selected patients, as well as reporting on different patient series in the international literature [7, 8]. Though the mainstream suggests the use of OPHLs in cT2-T3 N0-N1 LCs not eligible for TLM (due to suboptimal laryngeal exposure or borderline extension to certain delicate areas like pre-epiglottic and/or paraglottic spaces), for which the use of adjuvant therapy is not expected at all [9, 10], others reported remarkable oncologic and functional outcomes even for more advanced lesions such as cT3 with arytenoid fixation or frank T4a for anterior extension through the thyroid cartilage [8]. Clearly, when applied to such advanced LCs as an alternative to TL or CRT, OPHLs present the risk of needing adjuvant treatments once the final pathologic report shows adverse risk factors like gross thyroid cartilage invasion, close margins, pN > 2a, extranodal extension, or presence of both perineural (PNI) and lympho-vascular invasion (LVI). To date, controversies still persist in the surgical and scientific communities regarding the possibility to perform OPHLs when potentially at risk for adjuvant treatments, mainly due to the still poorly described side effects of (C)RT on the healing process after partial laryngectomies.

The purpose of the present study was, therefore, to evaluate the consequences of adjuvant therapies on laryngeal function after OPHLs. Towards this end, we retrospectively collected the data of patients undergoing Type II and III OPHLs followed by adjuvant treatments in 8 Italian high-volume centers for LC, with the aim to assess the oncologic and functional outcomes obtained.

Materials and methods

Patients

Clinical charts of patients affected by LC and submitted between January 1995 and December 2017 to OPHL Types II and III followed by adjuvant (C)RT were collected from 8 Italian referral high-volume centers for laryngeal oncology. Inclusion criteria encompassed: patients affected by cT2-T4a LC not previously submitted to other surgical or non-surgical treatment(s) and never treated before for other head and neck cancers, completion of adjuvant (C)RT as suggested by the multidisciplinary tumor board without interruption or late start after surgery (> 3 months), and with a minimum follow-up of 2 years.

One-hundred and thirty patients fulfilled the above-mentioned criteria and were included in the study. Preoperative work-up consisted of endoscopic and imaging evaluation performed no more than 4 weeks before surgery. The diagnostic endoscopic work-up always included flexible videolaryngoscopy under local anesthesia to assess the superficial margins of the lesion under white light (WL) and, since 2005, Narrow Band Imaging (NBI, Olympus Medical System Corporation, Tokyo, Japan). Either computed tomography (CT) or magnetic resonance (MR) imaging was used for preoperative staging [11]. Neck ultrasound (US) with or without fine-needle aspiration cytology was routinely performed. Patients also received intraoperative rigid endoscopy with 0°, 30°, and 70° telescopes by WL and NBI under general anesthesia to obtain more information about tumor extension [12]. Selective (SND) or modified radical neck dissections (MRND) were performed simultaneously to the OPHL, in adherence with National Comprehensive Cancer Network guidelines for cT2-T4 LC [13]. Tumors were reclassified according to the 8th Edition of the TNM classification of malignant tumors [14]. We adhered to ELS guidelines for postoperative follow-up [15, 16].

Adjuvant therapy was indicated for pT4a tumors with gross extra-laryngeal extension, close or positive resection margins, > pN2a category, or presence of both PNI and LVI. A large volume encompassing the primary site and all the draining lymph nodes was irradiated with a dose of up to 54 Gy/2 Gy. Regions at higher risk for malignant dissemination received a 12 Gy boost (total 66 Gy/2 Gy; range, 62–68). If not contraindicated, platinum-based chemotherapy was offered to all patients with positive resection margins or extranodal spread, after proper clinical evaluation taking into account age and comorbidities.

Patients were defined as having "no evidence of disease" (NED) if alive and without recurrence at the last follow-up, "alive with disease" (AWD) if alive with

recurrence, "died of disease" (DOD) in case of LC-related death, and "died from other causes" (DOC) when death occurred for any other reason than LC. Our primary endpoint was the presence of tracheostomy and/or gastrostomy at the last follow-up visit (range, 24–188 months), with ensuing calculation of 5-year laryngo-esophageal dysfunction-free survival (LEDFS), defined as survival with a functional neolarynx, i.e., without tracheostomy and/or gastrostomy.

The Ethic Committee's approval for this study was deemed necessary at our Institutions after formal request to the appropriate parties.

Statistical analysis

Data are summarized as percentages for categorical data, or means, median, standard deviation and interquartile range (IQR) for quantitative data. A Cox regression was carried out to model the survival time, based on the following covariates: gender, intervention, disease stage, presence of tracheostomy and/or gastrostomy at the last follow-up visit. Statistical analysis was repeated using the variables significant to the previous processing as covariates. The Kaplan–Meier method was then applied, with Log Rank test, divided by tracheostomy and disease stage. Associations between categorical data were evaluated with the Chi-square test or, when appropriate, Fisher's exact test. SPSS-IBM package for Mac OS was used. The statistical significance threshold level was set at $p < 0.05$.

Results

We collected data on 130 patients (116 males, 14 females). Mean age of the study cohort was 60.8 ± 8.9 years (median, 62; IQR, 13). Mean follow-up was 50.7 ± 39.4 months (median, 38; IQR, 51). The pathological TNM is summarized in Table 1.

Adjuvant therapy consisted of CRT in 53 (41%) patients and RT alone in 77 (59%). Eighty percent of patients were submitted to an OPHL Type II, whereas 20% of cases underwent OPHL Type 3. In 75% of cases one arytenoid was resected, and in 42% the resection included the epiglottis. Overall, at the last follow-up visit, 69% of patients were NED, 4% AWD, 12% DOD, and 14% DOC. Thirteen percent of patients remained tracheostomy dependent and 3% maintained the gastrostomy in place. Five-year LEDFS was 85%, while 5-year overall (OS) and disease-free survivals (DFS) were 71.5% and 68%, respectively.

Cox's first regression to model survival time provided the survival function represented in Fig. 1. The only significant variable in predicting survival was tracheostomy ($p = 0.020$). When the analysis was repeated, using tracheostomy as the only covariate, statistical significance was confirmed ($p = 0.037$). The graph, divided according to patients with and without tracheostomy, is shown in Fig. 2. The Kaplan–Meier method was used, subdivided by the presence or absence of tracheostomy. Log Rank test showed that survival time of patients with tracheostomy was significantly lower ($p = 0.031$) than those without (Table 2). Finally, the Kaplan–Meier results, dividing the population into Stages

Table 1 Pathological TNM according to the 8th Edition of the AJCC-UICC Staging System

pN pT	0	1	2	3	Tot
2	3	4	4	1	12
3	15	15	36	1	67
4	31	5	15	0	51
Tot	49	24	55	2	130

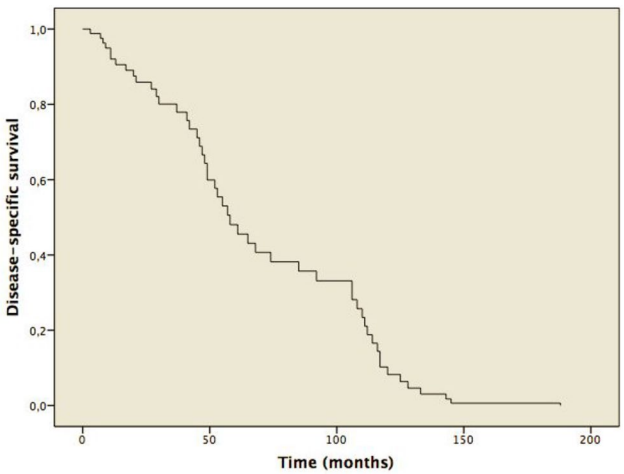

Fig. 1 Kaplan–Meier plot for disease-specific survival (DSS)

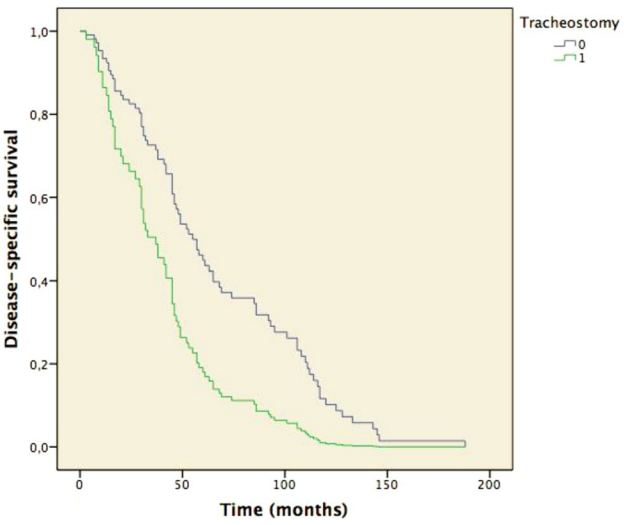

Fig. 2 Difference in patients with and without tracheostomy, with respect to disease-specific survival

Table 2 Mean value of disease-specific survival according to the variable tracheostomy

Tracheostomy	Mean survival time (months)	Standard error	95% confidence interval	
			Lower limit	Upper limit
No	66.10	4.91	56.48	75.73
Yes	41.27	9.30	23.05	59.49

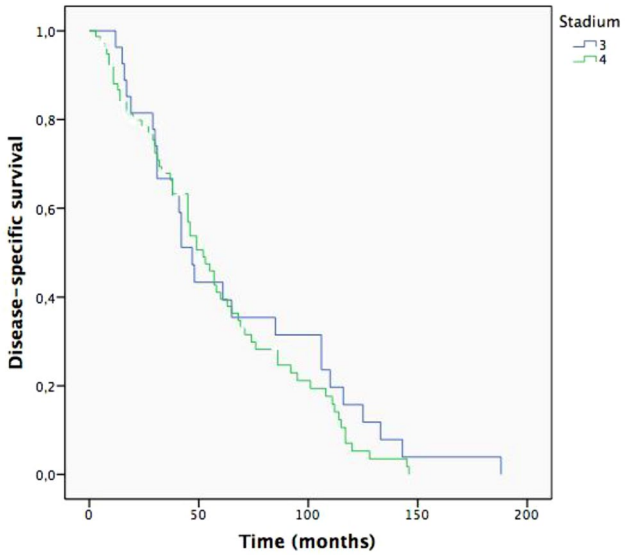

Fig. 3 Difference in Stage III and IV patients, with respect to disease-specific survival (DSS)

Table 3 Mean value of disease-specific survival according to the variable stage of disease

Stage	Mean survival time (months)	Standard error	95% confidence interval	
			Lower limit	Upper limit
3	66.19	9.42	47.73	84.65
4	59.09	4.77	49.75	68.44

III and IV, are shown in Fig. 3. The Log Rank test was not significant (Table 3).

The Chi-Square test showed a significant association between tracheostomy and type of OPHL performed ($p < 0.001$), as only 7.5% of subjects with OPHL Type II remained tracheostomy dependent, while 34% of those submitted to OHPL Type III maintained the tracheostomy (Fig. 4). In contrast, the correlation between tracheostomy and resection of one arytenoid, epiglottis, need for and modality of adjuvant therapy delivered (RT vs. CRT) did not show any significant association. Finally, the association between tracheostomy and stage of disease was not significant. When the correlation analysis was repeated by replacing the variable tracheostomy with gastrostomy, no

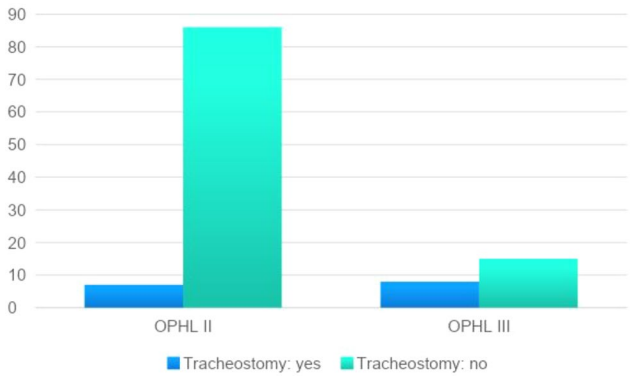

Fig. 4 Histograms of patients after OPHL Types II and III according to tracheostomy dependence

significant association was found, probably due to the small number of patients in this group.

Discussion

The potential for long-term survival among patients with advanced LC is nowadays significant and, consequently, the choice of the most adequate upfront treatment is essential for cancer control and optimization of subsequent functional outcomes. The role of OPHLs has been long debated in both surgical and non-surgical communities, especially when dealing with the controversial issue related to adjuvant (C) RT. In particular, Laccourreye et al. reported a rate of permanent gastrostomy and tracheostomy of 16.6% and 1.1%, respectively, after a minimum follow-up of 10 years [17]. Alterio and coworkers [18] found late severe laryngeal toxicity in 34% of patients, although with laryngeal and function preservation obtained in 93% and 81%, respectively. Buglione et al. [19] compared the outcomes of early supraglottic cancer treated by curative RT ($N = 132$) with those of a smaller group of 30 patients submitted to conservative surgery and postoperative RT, finding no difference in functional and oncologic outcomes. Even Costa et al., analyzing the outcomes of 532 patients with advanced supraglottic cancer treated by TL and RT, partial laryngectomies and RT, or RT alone, did not find significant functional differences between the latter two groups [20]. By contrast, a series from the National Cancer Institute of Milan, Italy, demonstrated some negative effects of postoperative RT on laryngeal functional outcomes, the most remarkable of which was a longer permanence of the tracheostomy in place [21].

Flaws of the present study include its retrospective nature and recruitment of patients treated in different centers within a relatively long-time period. Nonetheless, this can also reflect a pro of this work since it tends to eliminate (or reduce) referral and single-center biases. Moreover, the present multicenter series gathers a considerable

number of patients with advanced LCs treated by OHPLs and adjuvant (C)RT, with a follow-up adequately long and representative. The vast majority of patients included in the present study could have been considered unfit for OPHLs according to the most diffused guidelines, since frequently affected by T4a lesions or with $N > 1$. Such conditions, in many institutions, would have most probably directed these patients to non-surgical organ-preservation protocols or upfront TL. However, as herein demonstrated, even in such advanced cases, when properly selected based on adequate age, cardiovascular/pulmonary profiles, and good Karnofsky performance status, OPHL Types II and III followed by (C)RT provide a chance of favorable oncologic outcomes with adequate laryngeal function preservation. For comparison, indeed, an upfront CRT regimen typically achieves a 5-year OS around 60%, while the T4 subgroup usually presents values < 30% [22, 23]. In line with such an assumption, a recent review of the literature by Riga et al. [7] demonstrated that in T3 LC surgical management provides better survival and organ-preservation rates than non-surgical options. In 2019, Marchi et al. [10] published their series of 104 T3 LC treated by non-surgical regimens or surgery (TLM, OPHL, and TL). Both DFS and DSS were better in the surgical group as a whole, while LEDFS was superior in the TLM subgroup. Clearly, as in every non-randomized, retrospective series, patient selection undoubtedly biases the results, but the conclusion here is that, in absence of methods allowing virtual randomized surgical studies in an ethical way, they will be always conducted in a biased fashion, but still maintain their intrinsic value. As for every other complex surgical procedure, in fact, even for OPHL (with or without adjuvant treatments), the key element to achieve the best oncologic and functional results is represented by the wisest and most scrupulous selection of adequate patients to be submitted to such a procedure. Therefore, their random assignment to one or another treatment arm of a presumed randomized control trial will never be possible, if not totally unethical.

With the above-mentioned caveat, in our series, the T category was not significantly correlated with survival. The only significant prognosticator, indeed, was the presence of tracheostomy after treatment which, not surprisingly, was maintained more frequently in patients submitted to the more advanced form of OPHL (Type III). However, tracheostomy was not significantly correlated with T category. In fact, an OPHL Type II can be oncologically safe even for selected anterior T4a tumors, whereas a small posterior T3 can sometimes require an OPHL Type III. Moreover, it has been recently observed that "posterior" T3–T4 LCs (in respect to visceral spaces divided according to a coronal plane passing in front of the arytenoid vocal process, perpendicularly to the ipsilateral thyroid lamina) tend to have worse prognosis than the "anterior" ones [24].

Recent evidence suggests that T4 LC has better oncologic results after surgery [25, 26] and the updated guidelines of the ASCO Clinical Practice acknowledge this fact, recommending TL for large volume T4 tumors and/or patients with poor pre-treatment laryngeal functions. However, even though TL results in better survival and quality of life compared to CRT or RT alone [27], a subgroup of carefully selected patients might benefit from OPHL followed by (C)RT still achieving, as herein demonstrated, oncologic results that are at least comparable to those of TL, with all the advantages deriving from preservation of laryngeal function.

Nonetheless, some essential issues must be understood before erroneously assuming that such an organ-sparing approach could be safely applied to every advanced LC. In fact, in line with similar considerations for non-surgical organ-sparing strategies [1], if preservation of a functional larynx and normal swallowing after OPHL is of utmost importance, obtaining this with success must start from careful assessment of the causes and amount of arytenoid fixation. This element, together with other factors such as swallowing function and airway patency, plays a paramount role in defining a preoperative (and, even more, postoperative) functional larynx. In accordance with these findings, an editorial of international experts endorsed the belief that patients with little prospect of regaining laryngeal function (whether because of a lack of support, compliance issues, or extensive destruction of the laryngeal framework with deterioration of its physiologic functions) are poor candidates for non-surgical (and, for what concerns the present discussion, also surgical) laryngeal preservation strategies. For such patients, upfront TL should be strongly recommended [28].

Data regarding the impact of pre-treatment tracheostomy on OPHL oncological and functional outcomes are not very clear, as some authors have reported an adverse prognostic impact on survival [29, 30]. Moreover, there is a relatively unexplored field that refers to the real gain of adding (C)RT after surgery for T3-T4a LC. As opposed to the clear evidence that adjuvant treatments would definitively add toxicity [31, 32], up to 20% of T4a patients may have no survival improvement from such a policy [33]. Moreover, Chen reported that adjuvant therapy might offer survival benefits for intermediate-risk advanced stage cancers patients who are < 70 years old with T1–4 N2–3 disease, but might not in older ones or in those with T3–4 N0–1 LC. In this scenario, age would seem to play a crucial role in predicting survival outcomes [34]. Association of elderly age and inferior OS could reflect the higher non-cancer related mortality, but, on the other hand, a significantly worse DSS could be explained by suboptimal treatment choice due to age-related clinical and social features as already described in other studies [35, 36]. Finding which subgroup of OPHL patients, in whom

adjuvant (C)RT is indicated, would really benefit from these postoperative treatments will undoubtedly be of crucial importance to avoid useless toxicity and optimize resources for healthcare systems.

Conclusion

Patient selection before treatment of advanced LC must be wisely personalized, as there is no univocal therapeutic tool that can be applied as the optimal choice for all patients. This study underlines how, in a properly selected subgroup of patients affected by advanced LC, OPHL Types II and III, even when followed by adjuvant (C)RT, may be associated with favorable oncologic and functional outcomes.

Acknowledgments This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Funding Authors declare that they didn't receive any financial support.

Data availability The data that support the findings of this study are available from the corresponding author, RL, upon reasonable request.

Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests

Ethics approval The study was approved by the local Ethics Committee of the first author's (LM) affiliation.

References

1. Forastiere A, Lewin JS, Nathan CA et al (2018) Use of larynx-preservation strategies in the treatment of laryngeal cancer: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol 36:1143–1169
2. Majer E, Rieder W (1959) Technique de laryngectomiepermettant de conserver la perméabilitérespiratoire (la crico-hyoidopexie). Ann OtolaryngolChirCervicofac 76:677–681
3. Labayle J, Bismuth R (1971) Laryngectomietotale avec reconstruction. Ann OtolaryngolChirCervicofac 88:219–228
4. Pique JJ, Desaulty A, Decroix G (1974) Crico-hyoido-épiglottopexie. Technique opératoire et résultatsfonctionnels. Ann OtolaryngolChirCervicofac 91:681–689
5. Rizzotto G, Succo G, Lucioni M, Pazzaia T (2006) Subtotal laryngectomy with tracheoioidopexy: a possible alternative to total laryngectomy. Laryngoscope 116:1907–1917
6. Succo G, Peretti G, Piazza C et al (2014) Open partial horizontal laryngectomies: a proposal for classification by the working committee on nomenclature of the European Laryngological Society. Eur Arch Otorhinolaryngol 271:2489–2496
7. Riga M, Chelis L, Danielides V, Vogiatzaki T, Pantazis T, Pantazis D (2016) Systematic review on T3 laryngeal squamous cell carcinoma: still far from a consensus on the optimal organ preserving treatment. Eur J Surg Oncol 43:20–31
8. Succo G, Crosetti E, Bertolin A et al (2015) Benefits and drawbacks of open partial horizontal laryngectomies, part B: intermediate and selected advanced stage laryngeal carcinoma. Head Neck 33:649–657
9. Strojan P, Haigentz M Jr, Bradford CR et al (2013) Chemoradiotherapy vs. total laryngectomy for primary treatment of advanced laryngeal carcinoma. Oral Oncol 49:283–286
10. Marchi F, Filauro M, Missale, et al (2019) A Multidisciplinary team guided approach to the management of cT3 laryngeal cancer: a retrospective analysis of 104 cases. Cancers (Basel) 11(5):717
11. Maroldi R, Ravanelli R, Farina D (2014) Magnetic resonance for laryngeal cancer. CurrOpinOtolaryngol Head Neck Surg 22(2):131–139
12. Piazza C, Cocco D, Del Bon F, Mangili S, Nicolai P, Peretti G (2011) Narrow band imaging and high definition television in the endoscopic evaluation of upper aero-digestive tract cancer. Acta Otorhinolaryngol Ital 31:70–75
13. Colevas AD, Yom SS, Pfister DG et al (2018) NCCN Guidelines® insights head and neck cancers featured updates to the NCCN Guidelines. J Natl ComprCancNetw 16:479–490
14. Brierley JD, Gospodarowicz MK, Wittekind C et al (2017) TNM classification of malignant tumours, 8th edn. Wiley Blackwell, Oxford
15. Simo R, Bradley P, Chevalier D et al (2014) European Laryngological Society: ELS recommendations for the follow up of patients treated for laryngeal cancer. Eur Arch Otorhinolaryngol 271:2469–2479
16. Marchi F, Piazza C, Ravanelli M et al (2017) Role of imaging in the follow-up of T2–T3 glottic cancer treated by transoral laser microsurgery. Eur Arch Otorhinolaryngol 274(10):3679–3686
17. Laccourreye O, Hans S, Borzog-Grayeli A, Maulard-Durdux C, Brasnu D, Housset M (2000) Complications of postoperative radiation therapy after partial laryngectomy in supraglottic cancer: a long term evaluation. Otolaryngol Head Neck Surg 122:752–757
18. Alterio D, Ansarin M, Jereczek-Fossa BA et al (2013) What is the price of functional surgical organ preservation in local-regionally advanced supraglottic cancer? Long term outcome for partial laryngectomy followed by radiotherapy in 32 patients. Tumori 99:667–675
19. Buglione M, Pedretti S, Costa L et al (2015) Clinical outcomes and toxicity after exclusive versus postoperative radiotherapy in supraglottic cancer: new solutions for old problems? The case of stage I and II disease. Radiol Med 120(11):1071–1077
20. Costa L, Pedretti S, Foscarini F et al (2016) Clinical outcomes and toxicity after exclusive versus postoperative radiotherapy in supraglottic cancer: new solutions for old problems? The case of stage III and IV disease. Radiol Med 121(1):70–79
21. Guzzo M, Ferraro L, Rezzonico S et al (2011) Open organ preservation surgery of the larynx: experience of IstitutoNazionale-Tumori of Milan. Head Neck 33(5):673–678
22. Forastiere AA, Zhang Q, Weber RS et al (2013) Long-term results of RTOG 91–11: a comparison of three nonsurgical treatment strategies to preserve the larynx in patients with advanced laryngeal cancer. J Clin Oncol 31:845–852
23. Forastiere AA, Goepfert H, Maor M et al (2003) Concurrent chemotherapy and radiotherapy for organ preservation in advanced laryngeal cancer. N Engl J Med 349:2091–2098
24. Del Bon F, Piazza C, Lancini D, et al (2019) Open partial horizontal laryngectomies for T3-T4 laryngeal cancer: Prognostic impact of anterior vs. posterior laryngeal compartmentalization. Cancers (Basel) 11(3): E289
25. Dyckhoff G, Plinkert PK, Ramroth R (2017) A change in the study evaluation paradigm reveals that larynx preservation compromises survival in T4 laryngeal cancer patients. BMC Cancer 17:609
26. Al-Gilani M, Skillington SA, Kallogjeri D, Haughey B, Piccirillo JF (2016) Surgical vs. non surgical treatment modalities for T3

glottic squamous cell carcinoma. JAMA Otolaryngol Head Neck Surg 142:940–946
27. Al-Mamgani A, Navran A, Walraven I, Schreuder WH, Tesselaar MET, Klop WMC (2019) Organ-preservation (chemo)radiotherapy for T4 laryngeal and hypopharyngeal cancer: is the effort worth? Eur Arch Otorhinolaryngol 276(2):575–583
28. Beitler JJ, Ridge JA, Vermorken JB et al (2018) T4 laryngeal cancer with good function: should we be reluctant to treat without surgery? Int J Radiat Oncol Biol Phys 102(5):1400–1403
29. Mendenhall WM, Parsons JT, Mancuso AA, Pameijer FJ, Stringer SP, Cassisi NJ (1997) Definitive radiotherapy for T3 squamous cell carcinoma of the glottic larynx. J Clin Oncol 15:2394–2402
30. MacKenzie R, Franssen E, Balogh J, Birt D, Gilbert R (1998) The prognostic significance of tracheostomy in carcinoma of the larynx treated with radiotherapy and surgery for salvage. Int J Radiat Oncol Biol Phys 41:43–51
31. Giacalone NJ, Qureshi MM, Mak KS et al (2017) Adjuvant chemoradiation does not improve survival in elderly patients with high-risk resected head and neck cancer. Laryngoscope 128:831–840
32. Pellini R, Mercante G, Marchese C, Terenzi V, Sperduti I, Manciocco V, Ruscito P, Cristalli G, Marchesi P, Pichi B, Spriano G (2013) Predictive factors for postoperative wound complications after neck dissection. Acta Otorhinolaryngol Ital 33(1):16–22
33. Li M, Zhang T, Tan B, Yu M, Zhang B (2019) Role of postoperative adjuvant radiotherapy for locally advanced laryngeal cancer: a meta-analysis. Acta Otolaryngol 139:172–177
34. Chen MM, Colevas AD, Megwalu U, Divi V (2018) Survival benefit of post-operative chemotherapy for intermediate-risk advanced stage head and neck cancer differs with patient age. Oral Oncol 84:71–75
35. Sanabria A, Carvalho A, Vartanian J, Magrin J, Ikeda M, Kowalski L (2007) Factors that influence treatment decision in older patients with resectable head and neck cancer. Laryngoscope 117:835–840
36. Kanwar A, Hutcheson KA, Ghosh A et al (2018) Age-adjusted comorbidity and survival in locally advanced laryngeal cancer. Head Neck 40:2060–2069

Authors and Affiliations

Luca Muscatello[1] · Cesare Piazza[2,3] · Giorgio Peretti[4] · Filippo Marchi[4] · Andy Bertolin[5] · Erika Crosetti[6] · Gianluca Leopardi[7] · Riccardo Lenzi[8] · Laura Manca[9,10] · Jacopo Matteucci[8] · Raul Pellini[11] · Gerardo Petruzzi[11] · Livio Presutti[12] · Antonio Sarno[13] · Giovanni Succo[6] · Sara Valerini[12] · Giuseppe Rizzotto[5]

1 Unit of Otorhinolaryngology, Azienda USL Toscana Nord Ovest, Versilia Hospital, Camaiore (LU), Italy

2 Department of Otorhinolaryngology, Maxillofacial and Thyroid Surgery, Fondazione IRCCS, National Cancer Institute of Milan, Milan, Italy

3 Department of Oncology and Oncohematology, University of Milan, Milan, Italy

4 Department of Otorhinolaryngology, Head and Neck Surgery, University of Genoa, Genoa, Italy

5 Otolaryngology Service, Vittorio Veneto Hospital, Vittorio Veneto (TV), Italy

6 Head and Neck Oncology Service, Candiolo Cancer Institute, FPO IRCCS, Candiolo (TO), Italy

7 Unit of Otorhinolaryngology, Azienda USL Toscana Centro, San Giuseppe Hospital, Empoli (FI), Italy

8 Unit of Otorhinolaryngology, Azienda USL Toscana Nord Ovest, Apuane Hospital, Via E. Mattei 31, 54100 Massa, Italy

9 Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy

10 Department of Mathematics, University of Pisa, Pisa, Italy

11 Department of Otolaryngology, Head and Neck Surgery, IRCCS Regina Elena National Cancer Institute, Rome, Italy

12 Department of Otolaryngology, Head and Neck Surgery, University of Modena and Reggio Emilia, Policlinico Di Modena, Modena, Italy

13 Unit of Otorhinolaryngology, Azienda USL Toscana Centro, Santo Stefano Hospital, Prato, Italy