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Transoral Laser Microsurgery for Glottic Cancer in Patients Over 75 Years Old

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Objectives/Hypothesis: Laryngeal squamous cell carcinoma (LSCC) has a non-negligible incidence in elderly patients. However, there is still no clear indication on the ideal treatment for early-intermediate glottic LSCC in this specific age group. Both surgical and nonsurgical approaches may be burdened by complications and sequelae that negatively impact patient's health. In this setting, carbon dioxide transoral laser microsurgery (CO_2 TOLMS) is a promising minimally invasive treatment option.

Study Design: Retrospective case series in a single tertiary academic institution.

Methods: Patients who underwent CO_2 TOLMS for Tis-T3 glottic LSCC from 1997 to 2017 were reviewed. Demographic, clinical, and tumor characteristics, as well as postoperative complications were recorded. Overall (OS), disease-specific (DSS), recurrence-free (RFS), laryngo-esophageal dysfunction free survivals (LEDFS), and organ preservation (OP) were calculated.

Results: A total of 134 patients (mean age, 80 ± 4 years; median, 79; range, 75–93) were included in the study. Seven lesions were classified as pTis, 65 as pT1a, 22 as pT1b, 35 as pT2, and 5 as pT3. No treatment-related death was observed. Twenty-eight (20.9%) patients reported 10 surgical and 19 medical complications. Five-year OS, DSS, RFS, LEDFS, and OP were 68.9%, 95.4%, 79.5%, 66%, and 92.5%, respectively. Age and comorbidities were associated with OS and LEDFS. Advanced T categories were negatively correlated with OS, DSS, RFS, LEDFS, and OP. Age and comorbidities were not significant risk factors for complications.

Conclusions: CO_2 TOLMS can be considered a valuable therapeutic approach for selected Tis-T3 glottic LSCC even in the elderly given its favorable oncologic outcomes and minimal aggressiveness.

Key Words: Laryngeal cancer, glottis, transoral surgery, laser, elderly, oncologic outcome, complication.

Level of Evidence: 4

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INTRODUCTION

Laryngeal squamous cell carcinoma (LSCC) represents about 0.7% of all human malignant tumors and, after lung cancer, is the second most frequent neoplasm of the respiratory tract. The glottis represents the most commonly involved site, and the typical patient is male, in the sixth-seventh decade of life. However, patients aged 75 years or older still comprise a significant proportion of the affected population.[1,2] Advanced age is a well-known risk factor for cancer and can be associated with a reduction of multiorgan function and increased comorbidities. Nonetheless, thanks to general improvement of quality of life in industrialized countries, chronological age often does not directly correspond to the patient's biological profile and general health status. As a consequence, whenever possible, greater consideration should be given in applying the principles of minimally invasive treatments, coupled with appropriate oncologic follow-up,[3] in this group of patients.

Regarding early glottic carcinomas (stages I–II according to the AJCC-UICC TNM 8th Edition),[4] there is general agreement that the best treatment option should follow the principles of organ preservation.[5] For this reason, the therapeutic approaches more frequently used are carbon dioxide transoral laser microsurgery (CO_2 TOLMS according to the nomenclature proposed by Remacle et al.)[6] and radiotherapy (RT). Both treatments show similar survival and recurrence rates, making their choice in a multidisciplinary environment challenging and often debated. In particular, in potentially frail and elderly patients, the specialist should orient the choice of treatment with focus on reducing its impact on general health status (i.e., minimize complications and functional sequelae that affect quality of life). Currently, in patients

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older than 75 years, it is more common to opt for a non-surgical strategy even if clear evidence of treatment superiority is lacking. Moreover, only very few reports discuss CO_2 TOLMS treatment of LSCC in elderly patients,[7–9] with particular attention on extreme age.

The present work analyzes surgical and oncologic outcomes of CO_2 TOLMS for Tis-T3 glottic carcinomas in a homogeneous cohort of elderly patients treated at a single tertiary academic center.

MATERIALS AND METHODS

Data Collection and Study Population

A retrospective medical chart review was conducted among patients who underwent CO_2 TOLMS for glottic LSCC from January 1997 to December 2017 at the Unit of Otorhinolaryngology-Head and Neck Surgery, ASST-Spedali Civili of Brescia, University of Brescia, Italy. The study was performed following the principles of the Declaration of Helsinki and was approved by the Research Review Board, Ethics Committee, of the ASST Spedali Civili of Brescia, Italy (NP 4267).

Selection criteria were:

- Age ≥75 years;
- Glottic LSCC categorized as pTis-pT3 (according to the AJCC-UICC TNM 8th Edition)[4];
- Treatment by CO_2 TOLMS with curative intent;
- At least 2 years of follow-up.

Data on previous treatments were collected. Clinical preoperative examination was performed and recorded by high definition videolaryngoscopy and videolaryngostroboscopy. In case of clinical suspicion or risk of deep infiltration (i.e., significant anterior and/or posterior commissure involvement, impairment of vocal cord motility, subglottic spread), a radiological investigation was performed using computed tomography or magnetic resonance imaging. Medical comorbidities were evaluated and quantified using the American Society of Anesthesiology (ASA)[10] and the Adult Comorbidity Evaluation 27 (ACE-27) scores.[11]

Surgical Treatment and Histologic Examination

All patients underwent CO_2 TOLMS under general anesthesia after orotracheal intubation and adequate laryngeal exposure. Tumor resection was categorized following the European Laryngological Society (ELS) classification of cordectomies,[12,13] using en-bloc or multi-bloc resection according to specific tumor features, extension, and laryngeal exposure. Types of cordectomy and operative times were recorded.

Frozen sections were not routinely employed according to our institutional protocol, based on the strict collaboration with our head and neck surgical pathologists, directly involved in the evaluation of each cordectomy specimen. In particular, we preferentially resected additional margins after excision of the main specimens, which were then evaluated by the pathologist on permanent section. This procedure was employed in T2 to T3 bulky tumors requiring multi-bloc, three-dimensionally complicated resections. Positive surgical margins were managed following a standardized policy: patients with a single superficial positive margin had an indication for close follow-up; conversely, in case of multiple superficial and/or deep margin involvement, re-resection was proposed unless not feasible due to anatomical constrains or poor general status.[14] In this setting, RT was proposed only after repeated surgical procedures for recurrent superficial lesions or in case of deeply infiltrating tumors (i.e., pT3), in which patients could not tolerate an open partial horizontal laryngectomy (OPHL) and/or refused total laryngectomy (TL).

Postoperative Course and Follow-Up

Complications occurring during hospitalization or within the first 30 postoperative days were evaluated and subgrouped as surgical and medical. Complications were further classified according to the Clavien-Dindo classification.

A standardized follow-up policy through clinical evaluation with videolaryngoscopy was used in each patient. In case of lesions staged as pT2 to pT3, imaging was also conducted every 6 months for the first 2 years and once a year from the third to the fifth year.[15]

Outcomes and Statistical Analysis

Demographic, clinical, tumor, and follow-up data were collected in a single database. Survival curves were calculated using the Kaplan–Meier method. Two and 5-year overall (OS), disease-specific (DSS), recurrence-free (RFS), laryngo-esophageal dysfunction free survivals (LEDFS), and organ preservation (OP) were investigated.

For the analysis of OS, death for every cause was considered as an event. In DSS, patients who died of unrelated causes were considered as censored observations at the date of death. The endpoint for RFS was the date of the first recurrence. Patients who died without recurrence were considered as censored observations at the date of death. LEDFS was defined as survival without laryngectomy, tracheostomy, gastrostomy, and/or nasogastric feeding tube (NGFT). The endpoint for OP was the date in which patients underwent TL. Prognostic influence on OS, DSS, RFS, LEDFS, and OP was tested by univariate analysis for the recorded variables (i.e., ASA, ACE-27 scores, and pT category). Surgical and medical complications were matched to patients and surgical data to determine a statistical significance through univariate analysis. Statistical analysis was performed using the STATA 13 software (StataCorp. 2013. Stata Statistical Software: Release 13. College Station, Texas: StataCorp LP).

RESULTS

A total of 134 patients were included in the study. Mean age was 80 ± 4 years (median, 79; range, 75–93), while the male to female ratio was 9:1. Patients were divided into two groups according to age at surgery: middle-old (75–84 years; N = 111) and oldest-old (85 years and older; N = 23). Patients were categorized according to the preoperative anesthesiologic evaluation as ASA 2 in 62 (46.3%) cases, ASA 3 in 64 (47.7%), and ASA 4 in 8 (6%). Considering the ACE-27 comorbidity scoring system, patients were divided as follows: 23 (17.2%) score 0, 58 (43.3%) score 1, 49 (36.5%) score 2, and 4 (3%) score 4. Twenty-two (15.5%) patients had undergone previous treatments for laryngeal diseases elsewhere before referring to our institution. In detail, 9 (6.7%) patients underwent CO_2 TOLMS for malignant or premalignant glottic lesions, and 3 (2.2%) transoral surgery for benign pathologies.

According to the ELS classification, 2 (1.5%), 40 (29.5%), 19 (14.2%), 4 (3%), 64 (47.8%), and 5 (3.7%) patients underwent Types I, II, III, IV, V, and VI cordectomy, respectively. Mean operative time was

60.5 ± 39.6 minutes (median, 55; range, 20–370). At histopathology, 7 (5.2%) lesions were classified as pTis, 65 (48.5%) as pT1a, 22 (16.4%) as pT1b, 35 (27.1%) as pT2, and 5 (3.7%) as pT3. T category according to the age-group is detailed in Table I. No patient had nodal metastases at presentation.

Forty-five (33.6%) patients had at least one positive resection margin. Among these, 2 (4.4%) underwent CO_2 TOLMS revision surgery for deep or multiple superficial positive margins (re-resection was negative in one case and positive for SCC in the other). Two (4.4%) patients with deep and superficial positive margins underwent adjuvant RT. In 14 (31.2%) cases, histologic examination revealed two superficial positive margins and, considering patient age and comorbidities, a close follow-up policy was adopted. The residual 27 (60%) patients presenting just one superficial positive margin were followed-up as per institutional policy.

No treatment-related death was observed. Overall, 28 (20.9%) patients reported 29 postoperative complications. In detail, 10 (7.5%) had complications directly related to the surgical procedure: 5 experienced postoperative bleeding (requiring surgical revision in 4), 4 subsequently developed anterior glottic webs that significantly impaired airway patency and required surgical revision during follow-up, and one presented with cervical subcutaneous emphysema (undergoing spontaneous resolution within 36 hours). Nineteen medical complications were also reported in 18 (13.4%) patients, as detailed in Table II. According to the Clavien-Dindo classification, complications were defined as grade I (any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic and radiological interventions) in 8 (6%) patients, grade II (requiring pharmacological treatment with drugs other than such allowed for grade I complications) in 22 (16.4%), and grade IIIb (requiring surgical, endoscopic or radiological intervention under general anesthesia) in 8 (6%).

The mean postoperative hospitalization time was 3.8 ± 2.3 days (median, 3; range, 1–18). Hospitalization time was significantly increased in patients that encountered postoperative complications (5.6 vs. 3.4 days; $P < .001$).

A NGFT was positioned in 3 (2.2%) patients and maintained for a mean of 6.3 days (range, 4–8). No patient required tracheotomy at the time of the primary procedure; conversely, it was performed during revision for anterior glottic web in 2 (1.5%) patients who also received keel stent placement.

During follow-up, 13 of 89 patients (14.6%) with negative margins had local tumor recurrence. Of these, 6 (46.1%) were managed by a single CO_2 TOLMS. One (7.8%) patient was treated by CO_2 TOLMS for local recurrence and subsequent RT for a second recurrence. Six (46.1%) patients required TL for local recurrence that was not amenable to conservative strategies.

Similarly, 7 of 45 patients (15.6%) with positive margins had local tumor recurrence. Of these, 3 (42.9%) were managed by CO_2 TOLMS alone: 2 patients had a single recurrence, while the remaining patient experienced two relapses that were treated by CO_2 TOLMS. Four (57.1%) patients required TL for local recurrence that was not amenable to conservative strategies.

Overall, 115 (86%) patients required a single CO_2 TOLMS to manage the disease. Adjunctive transoral procedures were needed in six patients for relapse or positive margins needing re-resection (a single procedure in five patients and three procedures in one). Finally, eight patients needed revision surgery due to postoperative bleeding (N = 4) or late postoperative anterior web formation (N = 4).

Two-year OS, DSS, RFS, LEDFS, and OP were 86.6%, 100%, 88.2%, 82.3%, and 95.5%, respectively. Five-year OS, DSS, RFS, LEDFS, and OP were 68.9%, 95.4%, 79.5%, 66%, and 92.5%, respectively (Fig. 1). Survival rates according to the age group and pT category are detailed in Tables III and IV.

Margin status was not significantly associated with OS, DSS, RFS, LEDFS, or OP. Advanced age was only associated with decreased OS and LEDFS (both $P < .001$). High ASA scores were associated with worse OS and LEDFS ($P = .03$ and $P = .02$, respectively). Conversely, the ACE-27 comorbidity score was not associated with survival or recurrence.

Advanced T categories and types of cordectomy (Types IV–VI vs. Types I–III) were negatively correlated with OP ($P < .001$ and $P = .05$, respectively). Advanced T categories were also associated with reduced OS, DSS,

TABLE I.
pT Category According to Age Groups.

	Middle-Old No. (%)	Oldest-Old No. (%)
Tis	7 (5.2%)	0 (0%)
T1a	55 (41%)	10 (7.5%)
T1b	19 (14.2%)	3 (2.2%)
T2	25 (18.7%)	10 (7.5%)
T3	5 (3.7%)	0 (0%)

TABLE II.
List of Postoperative Medical Complications in the Entire Group of Patients (N = 134).

Medical Complications	No.
Hypertensive crisis	8
Emesis	3
Disorientation/delirium	2
Atrial fibrillation	1
Pulmonary embolism	1
Decreased oxygen saturation	1
Fever	1
Superficial venous thrombosis	1
Pneumonia	1

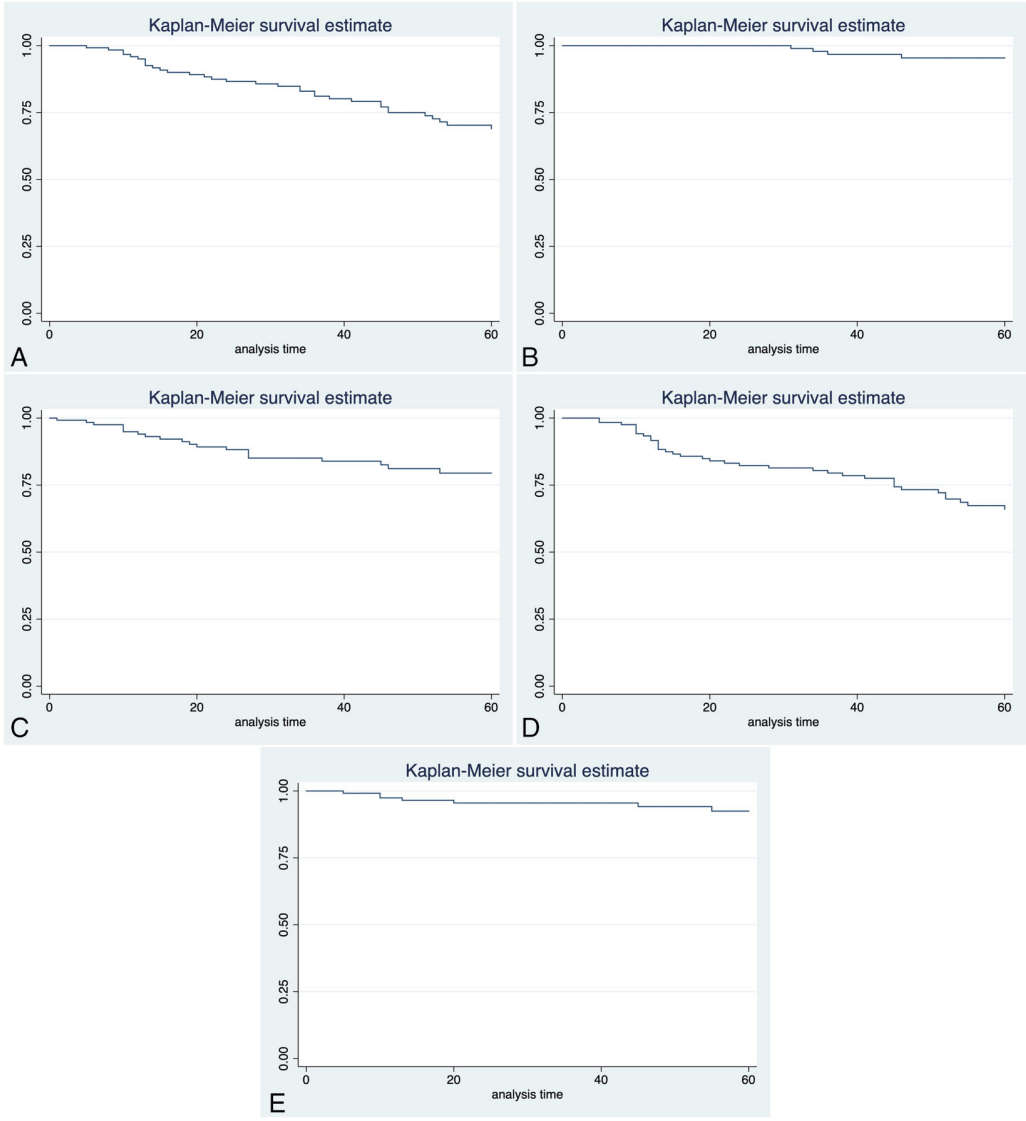

FIGURE 1. Kaplan–Meier curves showing OS (A), DSS (B), RFS (C), LEDFS (D), and OP (E) for the entire cohort. DSS = disease-specific; LEDFS = laryngo-esophageal dysfunction free survivals; OP = organ preservation; OS = Overall; RFS = recurrence-free. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

TABLE III.
Survival and Recurrence Outcomes According to Age Group.

	OS		DSS		RFS		LEDFS		OP	
	2-yr	5-yr	2-yr	5-yr	2-yr	5-yr	2-yr	5-yr	2-yr	5-yr
Middle-old	88.8%	74.0%	100%	94%	86.9%	76.9%	83.6%	70.6%	94.5%	91.1%
Oldest-old	75.6%	43.2%	100%	100%	94.4%	94.4%	75.6%	43.2%	100%	100%

DSS = disease-specific; LEDFS = laryngo-esophageal dysfunction free survivals; OP = organ preservation; OS = Overall; RFS = recurrence-free.

RFS, and LEDFS ($P = .05$, $P = .04$, $P = .01$, and $P < .01$, respectively).

Regarding the general complication rate, age and comorbidities did not represent a significant risk factor. On the contrary, T category ($P < .01$) was significantly associated with an increased overall complication rate.

DISCUSSION

In the present study, we analyzed a cohort of elderly patients affected by LSCC and treated by CO_2 TOLMS, focusing on the most advanced portion of the age spectrum (≥75 years, i.e., middle-old and oldest-old patients according to the US National Institute of Aging).[16]

TABLE IV.
Survival and Recurrence Outcomes According to pT Category.

	OS		DSS		RFS		LEDFS		OP	
	2-yr	5-yr	2-yr	5-yr	2-yr	5-yr	2-yr	5-yr	2-yr	5-yr
pTis-pT1	87.9%	76.3%	100%	98.5%	92.1%	87.6%	86.7%	74.7%	100%	97.9%
pT2	83.2%	43.8%	100%	82.5%	78.1%	58.2%	69.7%	37.7%	85%	78.5%
pT3	80%	60%	100%	100%	80%	53.3%	75%	50%	75%	75%

DSS = disease-specific; LEDFS = laryngo-esophageal dysfunction free survivals; OP = organ preservation; OS = Overall; RFS = recurrence-free.

Survival outcomes were satisfying, and patients mostly required only short-term hospitalization. Major complications were relatively rare (6% grade IIIb according to the Clavien-Dindo classification) and not associated with age or comorbidities. On the contrary, complications were mainly correlated with technical and disease-related factors (i.e., pT category). A NGFT was only rarely needed (2% of cases) and removed after a maximum of 8 days without residual dysphagia. This demonstrates the minimal impact of CO_2 TOLMS on deglutition, even after extensive resections, and the concrete possibility for early and comprehensive rehabilitation. No patient remained with a NGFT or tracheotomy-dependent.

The favorable complication profile of CO_2 TOLMS in the elderly has also been underlined by Sesterhenn et al.[17] and substantially parallels what has been observed in other age-mixed large series of patients treated by such a minimally-invasive approach.[18,19] In particular, the authors showed that significant complications appeared only in patients undergoing resection for supraglottic tumors or glottic lesions extending to the arytenoid, similarly to what has been shown in a previous report from our group dealing with the heavy functional burden associated with transoral supraglottic resections extending from the aryepiglottic fold to the arytenoid cartilage.[20] These data have been confirmed by Lucioni et al.[8] and Rodrigo et al.,[9] who reported minimal postoperative complications and sequelae in subjects over-65 and 70 years treated by CO_2 TOLMS for T1-T2 glottic LSCC. Similarly, Crosetti et al.[21] documented low rates of complications in patients over 70 years and treated by CO_2 TOLMS, especially when compared with those treated by open-neck procedures (i.e., OPHL and TL). In our experience, glottic cancer proved to be manageable with acceptable morbidity and limited functional sequelae even in a cohort of patients ≥75 years, resulting in 5-year DSS and LEDFS of 95.4% and 66%, respectively. In particular, the only patients showing laryngo-esophageal dysfunction in the medium- and long-term were those requiring TL for disease recurrence (5-year OP, 92.5%). A NGFT, when needed, was only maintained in the early postoperative period, and a tracheotomy was required only in case of revision surgery for late anterior synechiae that reduced airway patency. In this view, the non-negligible portion of patients developing a significant post-surgical anterior glottic web (3%) may be explained by the lower likelihood of performing staged procedures aimed at avoiding vocal fold synechiae in elderly patients for anesthesiologic concerns. However, this complication was always successfully managed by a revision procedure. Finally, the significant rate (33.6%) of positive margins in our series should be contextualized with the high frequency of false positivity of such an element (up to 80% in other Authors' experiences)[22,23] and the limited impact of microscopically positive margins on short and medium-term survivals, as also confirmed by our oncologic outcomes.

Previous reports have described the oncologic results of CO_2 TOLMS in elderly patients, attesting the limited impact of age.[24] However, age cut-offs varied among different studies (65 vs. 70 years) and did not allow direct comparison of survival outcomes. Therefore, our aim was to analyze a specific cohort at particularly high-risk, setting an advanced age cut-off to exclude the group defined as "young-old" (i.e., between 65 and 75 years)[16] which could lead to underestimation of the potential risks of CO_2 TOLMS in the "real" elderly population.

Furthermore, oncologic outcomes in patients over 75 years should be assessed considering the different variables typical of this age group. Surgeons treating elderly patients should take into account that other factors, such as frailty, comorbidities, performance, and cognitive status, are important considerations when predicting outcomes.[25] It is often required, in fact, to empirically balance on one side the anticipated timeframe/trajectory of mortality and morbidity risks related to LSCC, and, on the other, the ensuing treatment morbidity. Weighing these competing risks contextualizes a patient's treatment priorities within his/her entire life spectrum and time course of health needs.[26]

In particular, survival should not only be evaluated as an independent measure, but compared with the age-weighted life expectancy that can be retrieved from population studies or computed from national life tables.[27] The risks and outcomes of any treatment strategy should be weighted according to the patient's baseline expected survival, which, as already mentioned, is strictly dependent on age and comorbidities. Interestingly, the 2-year OS of our study cohort was comparable with that observed in the healthy general population of matched age and gender, as detailed in Table V. This comparison underlines the value of CO_2 TOLMS in the short- and medium-term management of LSCC in elderly patients, particularly given the acceptable rate of sequelae and complications observed.

As proposed by current guidelines,[5] the success of laryngeal preservation approaches in early-intermediate LSCC is higher when applying upfront conservative surgery than RT, while this may be secondary to patient

TABLE V.
Comparison Between 2-Year OS of the Present Series and That of the Matched Italian Population[27] According to Different Age Groups.

	2-Yr Overall Survival	
	Present Series (95% Confidence Interval)	General Population*
75–79 yr	92% (83–96)	93%
80–84 yr	78% (60–89)	87%
85–93 yr	76% (51–89)	71%

*Calculated outcomes based on Italian data (2019) and weighted according to a male to female ratio equivalent to that of the study cohort (9:1).

selection factors. Furthermore, according to these guidelines, in experienced hands, CO_2 TOLMS should be preferred because of similar or better outcomes compared with OPHL. Nonetheless, while age is defined as a critical factor for patient selection, there are no specific indications on the resulting changes in the treatment approach.

In a retrospective cohort of LSCC patients, Peters et al.[28] demonstrated by multivariate analysis that RT (compared to TL) and tumor stage were predictors of complications, but comorbidity and age were not. Furthermore, they reported that complications after CO_2 TOLMS were significantly lower than those after RT or TL in both the elderly and younger groups. In this view, the authors stated there is no reason to treat elderly LSCC patients differently than their younger counterparts. However, it is worth noting that the study did not include patients treated by OPHL, a procedure that has shown inferior functional results in patients over 65 years.[29–31]

In the United States, studies on LSCC have documented a progressively decreasing frequency of surgical therapy in the elderly, even if surgery has been associated with a reduced risk of overall mortality compared to non-surgical treatments.[32,33] Furthermore, according to an analysis of the Surveillance, Epidemiology, and End Results–Medicare database (2004–2007) by Gourin et al.,[34] chemoradiation in elderly patients with LSCC was associated with increased costs, additional cancer-directed treatment, and reduced likelihood of surgical salvage.

Finally, practical differences between CO_2 TOLMS and RT should be underlined and contextualized, namely: treatment timing, days of hospitalization, number of outpatient visits, and time-distribution of potential sequelae and complications. These factors are crucial in the middle-old and oldest-old patient groups because prolonged treatment protocols may be cumbersome for the patient and his/her caretakers from a physical and logistic standpoint. In this view, CO_2 TOLMS usually acts as an acute stressor: it consists of a procedure with short hospitalization time, and complications/sequelae appear in the initial phase and tend to resolve in the first weeks. Usually, the treatment consists in a single procedure. However, in a limited subgroup of patients, adjunctive surgeries may be needed because of complications, positive margins, and tumor recurrence, as well as complementary or salvage RT may be seldom required. On the other hand, primary RT is a more prolonged therapy that always requires frequent outpatient visits and sometimes even hospitalization. In this case, complications typically have a gradual onset and may be milder, but can last for weeks or months, potentially inducing incremental weight loss and compromising general health status, sometimes leaving long-term deficits. Especially in elderly patients, who might tolerate less toxicity than their younger counterparts,[35] these gradual disturbances may have a lasting impact on health and functional status. In this setting, assessment of functional reserve helps to predict the patient's tolerance to acute treatments, differentiating those at high risk for iatrogenic complications.

Regarding the limitations of this monocentric study, its retrospective design and relatively limited number of patients may have led to bias in the analysis of outcomes and their interpretation. In particular, an association between risk factors and outcomes may have been underestimated.

CONCLUSIONS

In the present study, we demonstrated that CO_2 TOLMS is a viable treatment option for Tis-T3 LSCC even in patients older than 75 years. The rate of surgical complication was limited and most patients needed only brief hospitalization. The functional results were optimal and no patient remained on NGFT or was tracheotomy-dependent. Finally, 2-year OS of our study cohort was comparable with that observed through life tables in the healthy general population of comparable age.

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REFERENCES

1. Howlader N, Noone AM, Krapcho M, et al., eds. *SEER Cancer Statistics Review, 1975-2017*. Bethesda, MD, https://seer.cancer.gov/csr/1975_2017/: National Cancer Institute; 2020.
2. Bradley PJ, Piazza C, Paderno A. A roadmap of six different pathways to improve survival in laryngeal cancer patients. *Curr Opin Otolaryngol Head Neck Surg* 2021;29:65–78.
3. Simo R, Bradley P, Chevalier D, et al. ELS recommendations for the follow-up of patients treated for laryngeal cancer. *Eur Arch Otorhinolaryngol* 2014;271:2469–2479.
4. Amin MB, Edge S, Greene F, et al., eds. *AJCC Cancer Staging Manual (8th edition)*. Springer International Publishing: American Joint Commission on Cancer; 2017.
5. Forastiere AA, Ismaila N, Lewin JS, et al. Use of larynx-preservation strategies in the treatment of laryngeal cancer: American Society of Clinical Oncology clinical practice guideline update. *J Clin Oncol* 2018;36:1143–1169.
6. Remacle M, Arens C, Eldin MB, et al. Laser-assisted surgery of the upper aero-digestive tract: a clarification of nomenclature. A consensus statement of the European Laryngological Society. *Eur Arch Otorhinolaryngol* 2017;274:3723–3727.
7. Ansarin M, Cattaneo A, Santoro L, et al. Laser surgery of early glottic cancer in elderly. *Acta Otorhinolaryngol Ital* 2010;30:169.
8. Lucioni M, Bertolin A, Rizzotto G, Accordi D, Giacomelli L, Marioni G. CO (2) laser surgery in elderly patients with glottic carcinoma: univariate and multivariate analyses of results. *Head Neck* 2012;34:1804–1809.
9. Rodrigo JP, García-Velasco F, Ambrosch P, et al. Transoral laser microsurgery for glottic cancer in the elderly: efficacy and safety. *Head Neck* 2019; 41:1816–1823.

10. Doyle DJ, Goyal A, Bansal P, Garmon EH. American Society of Anesthesiologists classification (ASA class). *StatPearls [Internet]*. Treasure Island (FL): StatPearls Publishing; 2021.
11. Paleri V, Wight R. Applicability of the adult comorbidity evaluation-27 and the Charlson indexes to assess comorbidity by notes extraction in a cohort of United Kingdom patients with head and neck cancer: a retrospective study. *J Laryngol Otol* 2002;116:200–205.
12. Remacle M, Van Haverbeke C, Eckel H, et al. Proposal for revision of the European Laryngological Society classification of endoscopic cordectomies. *Eur Arch Otorhinolaryngol* 2007;264:499–504.
13. Remacle M, Eckel HE, Antonelli A, et al. Endoscopic cordectomy. A proposal for a classification by the Working Committee, European Laryngological Society. *Eur Arch Otorhinolaryngol* 2000;257:227–231.
14. Fiz I, Mazzola F, Fiz F, et al. Impact of close and positive margins in transoral laser microsurgery for Tis-T2 glottic cancer. *Front Oncol* 2017;7:245.
15. Marchi F, Piazza C, Ravanelli M, et al. Role of imaging in the follow-up of T2-T3 glottic cancer treated by transoral laser microsurgery. *Eur Arch Otorhinolaryngol* 2017;274:3679–3686.
16. Aging UNIo. Why population aging matters. Available at: https://www.nia.nih.gov/sites/default/files/2017-06/WPAM.pdf.
17. Sesterhenn AM, Dünne AA, Werner JA. Complications after CO(2) laser surgery of laryngeal cancer in the elderly. *Acta Otolaryngol* 2006;126:530–535.
18. Vilaseca I, Nogues-Sabate A, Avilés-Jurado FX, et al. Factors of local recurrence and organ preservation with transoral laser microsurgery in laryngeal carcinomas; CHAID decision-tree analysis. *Head Neck* 2019;41:756–764.
19. Piazza C, Paderno A, Lancini D, et al. Long-term oncologic outcomes of 1188 Tis-T2 glottic cancers treated by transoral laser microsurgery. *Otolaryngol Head Neck Surg* 2021;194599820983727.
20. Piazza C, Barbieri D, Del Bon F, et al. Functional outcomes after different types of transoral supraglottic laryngectomy. *Laryngoscope* 2016;126:1131–1135.
21. Crosetti E, Caracciolo A, Molteni G, et al. Unravelling the risk factors that underlie laryngeal surgery in elderly. *Acta Otorhinolaryngol Ital* 2016;36:185–193.
22. Canis M, Ihler F, Martin A, Matthias C, Steiner W. Transoral laser microsurgery for T1a glottic cancer: review of 404 cases. *Head Neck* 2015;37:889–895.
23. Jumaily M, Faraji F, Osazuwa-Peters N, Walker RJ, Ward GM. Prognostic significance of surgical margins after transoral laser microsurgery for early-stage glottic squamous cell carcinoma. *Oral Oncol* 2019;97:105–111.
24. Carta F, Bandino F, Olla AM, Chuchueva N, Gerosa C, Puxeddu R. Prognostic value of age, subglottic, and anterior commissure involvement for early glottic carcinoma treated with CO_2 laser transoral microsurgery: a retrospective, single-center cohort study of 261 patients. *Eur Arch Otorhinolaryngol* 2018;275:1199–1210.
25. Korc-Grodzicki B, Downey RJ, Shahrokni A, Kingham TP, Patel SG, Audisio RA. Surgical considerations in older adults with cancer. *J Clin Oncol* 2014;32:2647–2653.
26. Smith GL, Smith BD. Radiation treatment in older patients: a framework for clinical decision making. *J Clin Oncol* 2014;32:2669–2678.
27. Italian National Institute of Statistics (ISTAT). Birth and mortality rates. Available at: https://www.asr-lombardia.it/asrlomb/en/tema/0205-natalit%C3%A0-e-mortalit%C3%A0-0. Accessed June 12, 2021.
28. Peters TT, van der Laan BF, Plaat BE, Wedman J, Langendijk JA, Halmos GB. The impact of comorbidity on treatment-related side effects in older patients with laryngeal cancer. *Oral Oncol* 2011;47:56–61.
29. Rizzotto G, Crosetti E, Lucioni M, et al. Oncologic outcomes of supratracheal laryngectomy: critical analysis. *Head Neck* 2015;37:1417–1424.
30. Schindler A, Pizzorni N, Mozzanica F, et al. Functional outcomes after supracricoid laryngectomy: what do we not know and what do we need to know? *Eur Arch Otorhinolaryngol* 2016;273:3459–3475.
31. Naudo P, Hans S, Laccourreye O, Laccourreye H, Weinstein G, Brasnu D. Functional outcome and prognosis factors after supracricoid partial laryngectomy with cricohyoidopexy. *Ann Otol Rhinol Laryngol* 1997;106:291–296.
32. Jean RA, Kallogjeri D, Strope SA, Hardin FM, Rich JT, Piccirillo JF. Exploring SEER-Medicare for changes in the treatment of laryngeal cancer among elderly medicare beneficiaries. *Otolaryngol Head Neck Surg* 2014;150:419–427.
33. Leachman B, DeMora L, Churilla TM, et al. Patterns of initial therapy for larynx cancer in elderly patients: a population based analysis. *Int J Rad Oncol Biol Phys* 2017;99:E404.
34. Gourin CG, Dy SM, Herbert RJ, et al. Treatment, survival, and costs of laryngeal cancer care in the elderly. *Laryngoscope* 2014;124:1827–1835.
35. Pignon T, Horiot J-C, Van den Bogaert W, Van Glabbeke M, Scalliet P. No age limit for radical radiotherapy in head and neck tumours. *Eur J Cancer* 1996;32:2075–2081.