

Functional and Oncologic Outcomes of Octogenarians Undergoing Transoral Laser Microsurgery for Laryngeal Cancer

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Abstract

Objective. To evaluate the oncologic and functional outcomes of transoral laser microsurgery (TLM) for glottic cancers in patients ≥ 80 years.

Study Design. Prospectively collected case series.

Setting. QEII Health Sciences Centre, Halifax, Canada.

Methods. This case series used a prospectively collected glottic cancer database to examine consecutive elderly patients (≥ 80 years old) undergoing TLM. Kaplan-Meier analysis was used to evaluate rates of disease-free, disease-specific, and overall survival as the primary end points of oncologic control. Secondary functional outcomes included voice function, length of hospital stay, and time to readmission.

Results. From 2005 to 2017, 17 octogenarian patients underwent TLM for glottic cancer. Median follow-up was 4.19 years (interquartile range, 0.71–6.95). Kaplan-Meier estimates of 5-year survival were 78.4% (disease free), 92.9% (disease specific), and 81.9% (overall). The median length of hospital stay was 1 day (range, 0–8). There was only 1 readmission within 30 days of surgery. No patients in this study developed significant surgical or postoperative complications requiring unplanned readmissions. Patient-perceived voice function improved to normal after treatment in 62.5% of patients.

Conclusion. The results of this study suggest that TLM is a safe and effective treatment modality for glottic cancer in patients aged ≥ 80 years, providing good oncologic control and satisfactory functional outcomes.

Keywords

transoral laser microsurgery, head and neck neoplasms, larynx cancer, geriatrics, frailty, complications, voice function, glottic cancer

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Laryngeal cancer is one of the most common cancers of the head and neck, with an increasing global burden in the past 3 decades.^{1,2} Globally, about 210,000 new cases and 126,000 deaths are reported annually.^{1,2} The incidence of laryngeal cancer peaks at the age of 65 years and gradually increases after the age of 80.^{1,2} Glottic cancers represent the majority of laryngeal cancers and typically arise from the anterior portion of the vocal cords.¹ Given the low rate of nodal spread and the early vocal change symptoms, glottic tumors can usually be diagnosed at an early stage, carrying good oncologic outcomes with 5-year survival of approximately 90% for stage 1 cancers and 80% for stage 2.¹

For patients with early-stage glottic cancers, transoral laser microsurgery (TLM) and radiotherapy are accepted standards of treatment with comparable efficacy and survival outcomes.^{3–6} The therapeutic decision remains multifactorial, depending on tumor phenotype, patient demographic, provider preference, and institutional capacity. Although the indication for TLM was initially limited to select patients, its use has expanded to include advanced lesions and older patients.^{5,7–9} TLM has shown favorable results over open surgery, including low complication rates and shorter functional recovery time.^{10,11} Similarly, TLM may provide improved functional outcomes and laryngeal preservation as compared with radiotherapy and chemotherapy, supporting the role of TLM in treatment of laryngeal cancers.^{4,5,12,13}

As the proportion of older populations increases with improvements in health care and higher cancer incidence with

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advancing age, the number of older patients with head and neck cancers has markedly increased. Although the evidence for TLM as the first-line treatment modality for laryngeal cancer is well established in middle-aged patients, oncologic control and tolerability of TLM for elderly patients are not sufficiently understood.⁹ As treatment options for older patients may involve additional consideration around prognoses and goals of care, more evidence for oncologic and functional outcomes is required to help guide decision making for physicians and patients.

The purpose of this study was therefore to assess oncologic outcomes for patients aged ≥ 80 years who underwent TLM for glottic cancer. The primary end points include overall survival (OS), locoregional control, and disease-specific survival (DSS). Secondary end points were postsurgical complications, sequelae, length of hospital stay, and need for unplanned readmission.

Methods

The reporting and analysis of this case series were completed according to the PROCESS guidelines (Consensus Preferred Reporting of Case Series in Surgery).¹⁴

Design

This study was a case series of a prospectively collected institutional TLM database comprising patients with glottic squamous cell carcinoma treated from January 2002 to November 2019 at the Queen Elizabeth II Health Sciences Centre, Halifax, Canada. All stages of glottic cancer were included. The collection of information within the database, as well as its use for this study, was approved by the Nova Scotia Health Authority Research Ethics Board. All participants of this study provided written informed consent. Details of data collection and information stored in the database have been described previously.¹⁵

Procedure

All patients underwent TLM resection. Two surgeons experienced in TLM were included in the study. Bouchayer or Kleinsasser laryngoscopes were used to provide adequate visualization of the tumor. With adequate exposure, the tumors were resected with a CO₂ laser, with all cases undergoing a tumor split approach. Following surgery, margin and main tumor samples were submitted for processing and pathologic characterization of the tumor. Adjuvant radiotherapy was offered to patients with recurrence or advanced disease at the discretion of the institutional multidisciplinary case review board.

Analysis

A descriptive analysis of patient demographic and complications was performed. All cancers were staged via the American Joint Committee on Cancer in use at the time of diagnosis. Patient comorbidity status was defined at the time of diagnosis with the Charlson Comorbidity Index (CCI).¹⁶ Smoking and alcohol consumption status at time of diagnosis was self-reported and categorized by frequency. Pre- and

postoperative voice function was collected through administration of the Voice Handicap Index–10 (VHI-10).¹⁷ The VHI-10 is a 10-item adaptation of the Voice Handicap Index, a health measurement instrument that measures patient-perceived voice outcomes and has been shown to be reliable and valid across a range of laryngeal pathologies, including glottic cancer.^{17,18} The VHI-10 is a subjective measurement of voice handicap in functional, physical, and emotional domains. Currently, there is no accepted minimal important clinical difference available for the VHI-10; however, scores >11 are considered to be abnormal.^{18,19}

Assessment of oncologic control was performed with Kaplan-Meier survival analyses, with disease-free survival (DFS), DSS, and OS as end points. DFS was defined as survival without locoregional recurrence or diagnosis of a new laryngeal tumor. Patients who were lost to follow-up were right censored at the time of last recorded visit.

Data analysis was performed with SPSS Statistics for Macintosh (version 26; IBM).

Results

From 2002 to 2019, 230 cases of glottic cancer were treated with TLM at our center. Of these, 20 patients were ≥ 80 years old, and 3 were excluded due to unavailability of patient information.

Between 2005 and 2017, 17 octogenarian patients (13 men and 4 women) underwent TLM for glottic cancer (**Table 1**). The median age was 82 years, ranging from 80 to 91. All patients had primary carcinomas. Tumor staging was as follows: 1 patient had carcinoma in situ, 7 T1a, 3 T1b, 4 T2, 1 T3, and 1 T4. Staging for the T3 tumor was determined preoperatively and confirmed with examination under anesthesia. Staging for the T4 tumor was initially considered cT2 preoperatively and subsequently upstaged intraoperatively. No patient had nodal involvement or metastatic disease. Three patients received adjuvant radiation: 1 patient with 2 recurrent tumors and 2 with advanced disease at T3 and T4. Regarding comorbidity burden, patients had a mean CCI score of 7.1, at a baseline of 6 with age ≥ 80 years (+4) and localized solid tumor (+2). Median duration of follow-up was 4.19 years (interquartile range, 0.71-6.94).

The median length of hospital stay was 1 day (range, 0-8). There was only 1 readmission within 30 days of surgery. Following discharge after TLM, 6 patients required further surgical management (35.3%): 3 for resection of recurrent tumors, 1 for resection of abnormal but histologically benign mucosa, 1 for resection of vocal cord adhesions, and 1 for planned adjuvant radiotherapy due to mobility and transportation concerns. No patients underwent an unplanned readmission. In this subcohort, the average time to repeat intervention was 208.5 days (range, 30-799).

Four patients developed complications following TLM resection. Three patients developed anterior glottic stenosis, and 1 developed glottic incompetence. Two patients with stenosis had minor webbing, and no functional deficits were noted. One patient developed stenosis with more involvement of the vocal folds and required TLM resection, which resulted

Table 1. Patient Demographics (n = 17).

Patient demographic	No. (%) ^a
Age, y ^b	82 (80.5-84.5)
Sex	
Male	13 (76.5)
Female	4 (23.5)
T stage	
Tis	1 (5.9)
T1a	7 (41.2)
T1b	3 (17.6)
T2	4 (23.5)
T3	1 (5.9)
T4	1 (5.9)
N stage	
N0	17 (100)
M stage	
M0	17 (100)
Charlson Comorbidity Index ^c	7.1 (1.1)
Smoking status	
Nonsmoker	3 (17.6)
Past smoker	13 (76.5)
<10 pack-year	1 (5.9)
>10 pack-year	7 (41.2)
Unknown history	5 (29.4)
Alcohol consumption per week	
0-6	15 (88.2)
7-14	1 (5.9)
Unknown	1 (5.9)
Adjuvant treatment	
None	14 (82.4)
Radiation	3 (17.6)

^aValues are presented as No. (%) unless noted otherwise.

^bMedian (interquartile range).

^cMean (SD).

in satisfactory voice outcome and airway patency. The patient with glottic incompetence received follow-up vocal fold augmentation via Radiesse injections, with adequate glottic closure and functional results. All patients recovered from postoperative complications. No patients developed intraoperative complications or required gastrostomy tube placement or tracheostomy tube insertion. No patients required total laryngectomy.

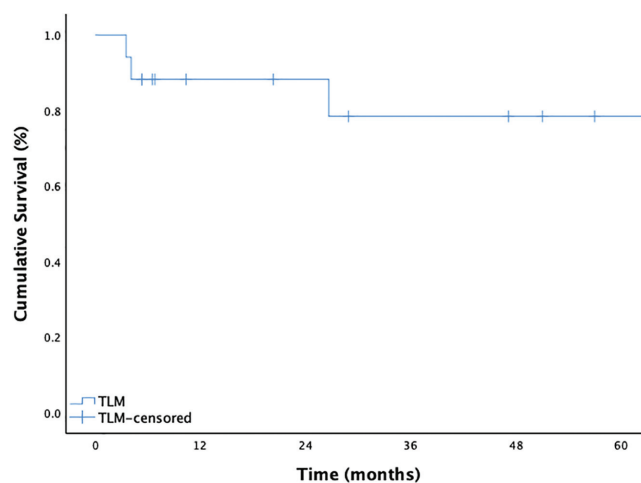
Postoperative vocal function measurements were available for 8 of 17 patients (47%; **Table 2**). In the postoperative period, 3 patients (37.5%) had VHI-10 scores >11, considered abnormal.¹⁸ Corresponding preoperative VHI-10 scores were available for 3 patients. In all 3 patients, vocal function improved following TLM. The average time point for VHI-10 measurement was 357.4 days.

There were 3 patients with locoregional recurrence or new primary cancers (**Figure 1**). One patient with a T1a tumor developed squamous cell carcinoma of the right lateral tongue after 3.5 months and underwent hemiglossectomy for resection

Table 2. Voice Handicap Index-10 Outcome.

Study ID	Voice Handicap Index-10		
	Preoperative ^a	Postoperative	Postoperative time point, d
TLMG-226		31	85
TLMG-062	16	10	95
TLMG-003	18	0	27
TLMG-137		12	384
TLMG-145		19	1349
TLMG-142		0	196
TLMG-148	2	0	200
TLMG-038		4	77

^aBlank cells indicate *not available*.



Time (months)	0	3.5	4.1	26.6
Remaining	17	16	15	8
Cumulative events	0	1	2	3

Figure 1. Kaplan-Meier analysis of disease-free survival. TLM, transoral laser microsurgery.

of the tumor. This patient died 6 years later due to an unrelated cerebrovascular event. The second patient with a T1a tumor developed a recurrent glottic tumor after 26 months, which was resected with TLM of the second tumor. This patient died of an unknown cause 7 years following the second resection. The third patient had a complex history of 3 recurrences of glottic cancer spanning >2 decades, receiving radiation therapy for the initial tumor and subsequent TLM resections for new primary tumors at 16- and 21-year time points. This patient developed a final recurrent tumor 25 years after the first tumor and was not a candidate for TLM due to advanced renal failure. He received radiation with curative intent and died 2 years later from chronic comorbidities. For glottic cancer treated with TLM resection, the Kaplan-Meier estimate of 5-year DFS was 78.4%.

During follow-up, 8 patients died (**Figure 2**). Five died from advanced comorbid diseases, including chronic renal

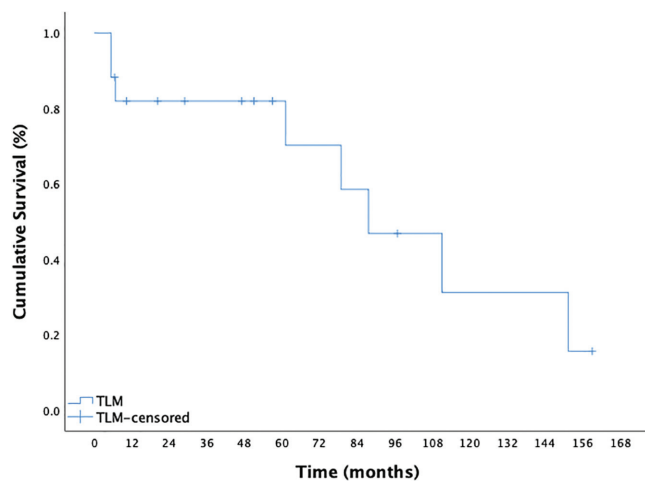


Figure 2. Kaplan-Meier analysis of overall survival. TLM, transoral laser microsurgery.

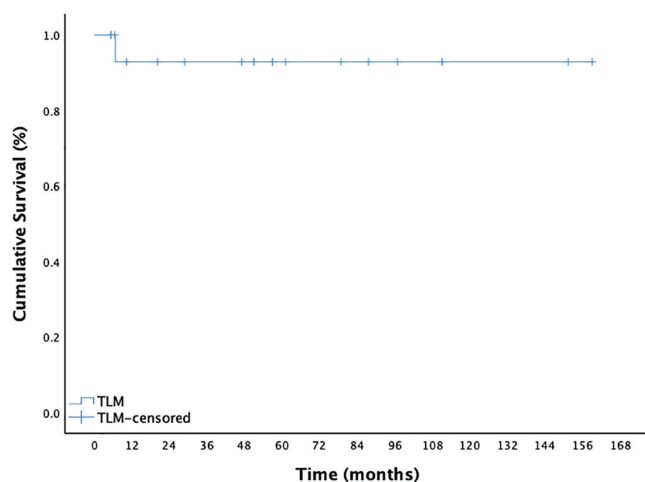


Figure 3. Kaplan-Meier analysis of disease-specific survival. TLM, transoral laser microsurgery.

failure, congestive heart failure, stroke, and *Clostridioides difficile* infection. Two patients died of unknown causes. There was 1 death due to disease, wherein the patient developed aspiration pneumonia following adjuvant radiation therapy and died during the course in hospital (**Figure 3**). For glottic cancer treated with TLM resection, Kaplan-Meier estimates of 5-year DSS and OS were 92.9% and 81.9%, respectively.

Discussion

The use of TLM has been increasingly accepted as a part of standard of care for laryngeal cancer in most tertiary centers.

TLM is a minimally invasive and effective management option, with recent studies showing improved oncologic and functional outcomes versus open surgery and primary radiotherapy.^{5,10} However, there is limited evidence currently available to adequately characterize the oncologic control, prognosis, and complications of TLM in elderly patients. This study bridges this knowledge gap by demonstrating excellent survival and functional outcomes in a cohort of consecutive octogenarians treated with TLM at our center.

For this study, the elderly patient population has been defined as ≥ 80 years of age. The conventional definition of elderly age has often been defined as >65 years²⁰; however, with increasing life expectancy and improved management of comorbidities, more patients >80 years old will access surgical treatment for head and neck cancers.^{21,22} Additionally, geriatric comorbidities are known to disproportionately increase at ≥ 80 years, with incidences of most conditions doubling from 65-69 years to ≥ 80 .^{21,23} Thus, assessment of the oncologic and surgical safety of TLM for glottic cancer in this older population engenders substantial clinical importance.

This study utilizes the CCI as a validated tool to assess comorbidity level with predefined comorbid conditions. This index provides a weighted summary measure based on adjusted risk of mortality that can be used to predict short- and long-term outcomes.¹⁶ Although CCI is a widely used scoring system, its limitations include differential prognostic value under binary variables and predefined comorbidities.²⁴ Moreover, for geriatric populations, mortality and postoperative complications may be better predicted by measures of frailty, such as the Frailty Index or Frailty Score,²⁵⁻²⁷ Frailty can be measured as the total number of health deficits with the Frailty Index or as limitations and dependence in activities of daily living with the Frailty Score and may be used to predict surgical candidacy in the elderly population. Ultimately, this process requires clinical judgment of the surgeons rather than an analysis of comorbidity burden.

Previous studies comparing age groups of patients who have undergone TLM for glottic neoplasms have demonstrated age as an important prognostic factor that significantly influences OS, DFS, and DSS.^{10,28-30} The average age of patients undergoing TLM is reported to be 65 to 68 years, with robust data showing efficacy and safety in this demographic.^{6,10} When patients with glottic cancer were stratified by age <65 and >65 years, Luo et al showed that older age was significantly associated with decreased OS, with a hazard ratio of 1.73.³¹ In a pooled retrospective study of elderly patients undergoing open laryngeal surgery and TLM, Crosetti et al correlated OS with patient age, with an OS of 64.0% in those aged 70-79 years and 33.9% in those ≥ 80 years.³⁰ Similarly, a large retrospective study of major head and neck surgery in age groups ranging from ≤ 49 to ≥ 80 years demonstrated that age itself did not significantly predict risk of complications in unadjusted analysis, but after adjustment for other risk factors, the ≥ 80 age group was associated with a higher odds of complications.³²

Age is an expected predictor of OS in elderly patients; nonetheless, this study provides support for effective oncologic control with TLM in patients ≥ 80 years old, as well as

additional evidence for the use of TLM in older patients. Rodrigo et al reported a 5-year DFS of 79% and 5-year OS of 68% in patients undergoing TLM for glottic cancer in their center (mean age, 76 years; range, 70-89). In a pooled analysis of 3 studies from their literature review of older patients undergoing the same procedure (mean age, 74.5 years; range, 65-95), they cited a 5-year DFS of $89\% \pm 5.6\%$ (mean \pm SD) and 5-year OS of $85.5\% \pm 2.6\%$.⁹ Djukic et al showed that DFS and OS were significantly lower in patients >75 years old than younger patients, at 72.7% for both 5-year rates.¹⁰ In a case series of patients >65 years, Lucioni et al reported 84.6% DFS during a mean \pm SD follow-up of 49.7 ± 23.2 months and 87.7% OS after 38.9 ± 17.2 months.³³

In this study, the use of TLM for glottic cancer was well tolerated in older patients, with 4 developing minor complications that had no significant long-term functional impacts and resolved with follow-up care. Notably, 1 patient did develop vocal cord adhesions that required additional resection. No patients developed intraoperative or significant postoperative complications, such as bleeding or tracheostomy. In other series, most common minor complications in older patients included postoperative glottic adhesion and granuloma, while more serious complications were hemorrhage, tracheostomy, and aspiration pneumonia.^{7,9,10,33}

For oncologic management in elderly patients, the quality of residual life is an important factor in guiding treatment decisions. The goals of care for many older patients focus on preserving functional status and maximizing time at home.³⁴⁻³⁶ Thus, secondary outcomes such as laryngeal preservation, voice function, and the burden of postoperative course are significant aspects of prognoses that should be considered by patients and care providers.³⁷ The collected VHI-10 data in this study show a positive trend in voice quality, although its statistical significance is limited. The patient burden of hospital visit remained low for older patients, with a postoperative short stay comparable to that of other centers, and most patients did not require revision surgery.⁹ A practical consideration for TLM is the less disruptive follow-up scheduling as compared with radiotherapy, as this patient population may experience additional mobility and transportation concerns.

In the context of the patients who were offered TLM for the treatment of glottic cancer, this cohort aged ≥ 80 years carried relatively lower rates of preexisting comorbidities, which indicate the main risk factor for survival and complications. Additionally, with chronic histories of smoking and alcohol consumption in a proportion of this patient population with head and neck cancers, the burden of secondary diseases increases. With a mean CCI of 7.1, these patients had a baseline of 6 (age ≥ 80 years and solid localized tumor) and 1 additional comorbidity on average. In epidemiologic studies of morbidity burden, the general population >80 years old was reported to have at least 3 chronic comorbid conditions on average. As an indication for TLM, patients must be well enough to undergo general anesthesia, which may exclude patients with complicated medical histories.

The findings of this study must be interpreted through its limitations. In this study, a small proportion of patients met the eligibility criteria. Additionally, comprehensive follow-up was lost to home or regional hospitals over the course of the study; however, the censored analysis suggests that TLM remains an effective mode of primary therapy for glottic cancer in elderly patients. Future studies comparing primary radiation and TLM for oncologic control as well as secondary functional outcomes with comprehensive voice data in this age group would help guide treatment decisions and patient expectations. Similarly, adjusted analysis—capturing more comprehensive comorbidity burden and frailty—to control for confounding is a key next step in exploring the use of TLM in elderly patients. Finally, our institution is a high-volume TLM center; thus, findings may not be generalizable to institutions with lower case volumes.

Conclusion

The results of this study indicate that TLM is a safe and effective option for the treatment of glottic cancer in patients ≥ 80 years of age with good preoperative performance status. Despite advanced age and comorbidities, elderly patients eligible for TLM can benefit from good oncologic control and optimistic quality-of-life factors.

Author Contributions

Changseok Lee, contributed to the design of the project and analysis and interpretation of the data, wrote the original manuscript, and assembled the final draft; has read and approved the final draft; **David Forner**, acquired data and provided significant feedback and revision for manuscript preparation; has read and approved the final draft; **Christopher W. Noel**, contributed to analysis and interpretation of data and critical manuscript revision; has read and approved the final draft; **Victoria Taylor**, contributed analysis and interpretation of data and critical manuscript revision; has read and approved the final draft; **Colin MacKay**, contributed to patient care, acquisition and analysis of the data, and critical manuscript revision; has read and approved the final draft; **Matthew H. Rigby**, contributed to patient care, acquisition and interpretation of data, and critical manuscript revision; has read and approved the final draft; **Martin Corsten**, contributed to patient care, acquisition and interpretation of data, and critical manuscript revision; has read and approved the final draft; **Jonathan R. Trites**, contributed to patient care, acquisition and interpretation of data, and critical manuscript revision; has read and approved the final draft; **S. Mark Taylor**, contributed to patient care, acquisition and interpretation of data, and critical manuscript revision; is the principal investigator and supervised this project; has read and approved the final draft.


Disclosures

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