

## ONCOLOGY

# Laser surgery of early glottic cancer in elderly

## *Il trattamento del carcinoma glottico in stadio iniziale nel paziente anziano*

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## SUMMARY

Aim of this retrospective study is to evaluate the impact of transoral laser surgery of early glottic cancer in elderly patients in terms of feasibility, disease-free survival, overall survival and organ preservation, in a single Institute (European Institute of Oncology). A total of 122 patients (male/female ratio 113/9), over 70s with untreated early stage glottic cancer, were consecutively evaluated and treated at the European Institute of Oncology from 2000 to 2008. None had contraindications to general anaesthesia and all patients signed informed consent to this surgical treatment. The severity of pre-operative comorbidities and the intra-operative risk were evaluated according to the American Society of Anaesthesiologists Grading Classification. All patients underwent laser cordectomies according to the European Laryngological Society classification. Histopathological examination demonstrated no evidence of tumour (pT0) in 19 patients (calculated only in patients with a previous vocal cord biopsy positive for squamous cell carcinoma), pTis in 18, pT1a in 53, pT1b in 16, pT2 in 14 and pT3 in 2, respectively. A 10-year overall survival, a tumour specific survival and a laryngeal tumour-specific survival were, respectively, 64.9%, 84.8% and 94.3%. In conclusion, transoral laser surgery is feasible in elderly patients with early stage glottic cancer, providing good results in terms of disease-free survival, organ preservation and quality of life. Our group of elderly patients had no intra-operative or post-surgical complications and resumed normal activities the day after discharge from hospital. Considering these factors, we can assess, that transoral laser surgery, therefore, represents a modern treatment that should be offered as an alternative to conventional radiotherapy in elderly patients with early glottic cancer referred to medical centres with expertise for this surgical procedure.

KEY WORDS: Early glottic cancer • Elderly patients • Transoral laser surgery

## RIASSUNTO

*Questo studio retrospettivo si propone di valutare l'impatto della chirurgia transorale nelle neoplasie glottiche in stadio iniziale nei pazienti anziani trattati in un singolo Centro (Istituto Europeo di Oncologia) in termini di fattibilità, sopravvivenza libera da malattia, sopravvivenza globale. Sono stati valutati 122 pazienti consecutivi (rapporto maschi/femmine 113/9), con età superiore od uguale ai 70 anni con neoplasia glottica non precedentemente trattata, senza controindicazioni all'anestesia generale, trattati presso l'Istituto Europeo di Oncologia dal 2000 al 2008. Tutti hanno firmato il consenso informato all'intervento endoscopico. La valutazione preoperatoria della gravità delle comorbidità e del rischio intra-operatorio, è stata valutata mediante la Classificazione della Società Americana di Anestesiologia (ASA). Gli interventi di cordectomia endoscopica sono stati eseguiti secondo la classificazione dell'European Laryngological Society. L'esame istopatologico definitivo non ha dimostrato evidenza di tumore (pT0) in 19 pazienti (dato calcolato solo nei casi precedentemente sottoposti a biopsia incisionale positiva per carcinoma a cellule squamose), pTis in 18 pazienti, pT1a in 53, pT1b in 16, pT2 in 14 e pT3 in 2 casi. La sopravvivenza globale a 10 anni, la sopravvivenza tumore specifica e quella tumore-laringeo specifica sono rispettivamente del 64,9%, 84,8 e 94,3%. In conclusione la chirurgia transorale endoscopica della laringe è proponibile nei pazienti anziani con tumore glottico in stadio iniziale, con buoni risultati, in termini di sopravvivenza libera da malattia, di preservazione d'organo e di qualità di vita. Il nostro gruppo di pazienti anziani non ha avuto complicanze intra- o post-operatorie e tutti hanno ripreso le loro normali attività il giorno dopo la dimissione dall'ospedale. Considerando questi fattori possiamo asserire che la chirurgia transorale dovrebbe essere il trattamento di scelta per le neoplasie glottiche in stadio iniziale anche nel paziente anziano, laddove esista l'attrezzatura e l'esperienza adeguata con questa metodica.*

PAROLE CHIAVE: Neoplasie glottiche in stadio iniziale • Pazienti anziani • Chirurgia transorale

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### Introduction

Early glottic cancer (Tis, T1a, T1b, T2) is one of the most curable malignancies in the head and neck, because not only the symptom of hoarseness allows an early diagnosis, but also, as a result of the glottis peculiar lym-

phatic drainage less than 1% of patients develop cervical metastasis. Laryngeal carcinoma makes up less than two percent of cancers worldwide, even though the incidence is increasing. In Italy and the rest of Europe, the populations are becoming older, and with ageing, the prevalence of cancer also increases: the skin and the aero-digestive

tract are the predominant cancers encountered in the elderly, and laryngeal squamous cell carcinoma must be expected to increase in the future <sup>1,2</sup>. Until recently, the borderline between middle and old age was 65 years <sup>3</sup>; the National Institute on Aging and the National Institute of Health have redefined the term “elderly”, placing it into three subcategories: “young old” for patients aged between 65 and 74 years, “older old” for patients aged between 75 and 85 years and “oldest old” for patients aged more than 85 years old <sup>4</sup>. Because elderly patients are characterized by age-specific problems, Socinski et al., offered a different definition: “old is when his health status begins to interfere with oncological decision-making guidelines” <sup>5</sup>. For these reasons, chronological age by itself cannot be considered the only criterion for the treatment planning decision: particularly nowadays, a Comprehensive Geriatric Assessment is highly recommended in geriatric oncology.

Today, external beam radiotherapy and transoral laser surgery (TLS) with CO<sub>2</sub> laser are the most common treatment modalities for early glottic cancer <sup>6</sup>. Radiotherapy is the most applied therapy worldwide, but since the early 1970s the advent of the CO<sub>2</sub> laser made transoral excision more and more popular. Several studies also suggested how open partial laryngectomies, such as supra-cricoid or fronto-lateral partial laryngectomy, can be employed as primary treatment modalities for early-intermediate-stage laryngeal cancer in elderly patients <sup>7</sup>. However, there is common consent that, in elderly patients, open partial laryngectomy should not be proposed as the first treatment option.

The principal aim of both radiation and surgical oncology is cancer cure, but before deciding the treatment schedule, it is important to know not only the patient’s wishes but also his life expectancy.

The aim of this study is to assess the impact of TLS in early-stage glottic cancer in terms of feasibility, disease-free survival, overall survival, organ preservation and cost benefit in elderly patients.

## Materials and methods

Between January 2000 and May 2008, 122 patients (male/female ratio 113/9; mean age, 74 years; age range 70-88 years) with early stage glottic cancer were treated at the Head and Neck Division at the European Institute of Oncology in Milan, Italy.

Many patients had different co-morbidities such as high blood pressure, coronary artery disease, chronic obstructive pulmonary disease, kidney disorders and others, presenting alone or in combination (Table I).

According to the American Society of Anaesthesiologists (ASA) score <sup>8</sup>, we divided our group of patients into four subgroups (Table I). Many patients were classified as ASA 2 (patient with mild systemic disease, 57 pts, 46.7%) or ASA 3 (patient with severe systemic disease, 50 pts, 41.0%).

**Table I.** Patient and tumour characteristics of patients treated with eTLS (n = 122 patients).

Characteristics	N (%)
<b>Age (Years)</b>	
Median (range)	74 (70-88)
<b>Sex</b>	
Males	113 (92.6)
Females	9 (7.4)
<b>Co-morbidity</b>	
None	1 (0.8)
Hypertension	23 (18.8)
Heart disease	18 (14.7)
COPD	5 (4.1)
Kidney	1 (0.8)
More than one	45 (36.9)
Other	29 (23.8)
<b>ASA score</b>	
1	11 (9.0)
2	57 (46.7)
3	50 (41.0)
4	4 (3.3)
<b>Clinical Stage (for glottic cancer)</b>	
T <i>in situ</i>	9 (7.4)
T1a	103 (84.4)
T1b	2 (1.6)
T2	8 (6.6)
<b>Pathological Stage (for glottic cancer)</b>	
T <i>in situ</i>	18 (14.7)
T0	19 (15.6)
T1a	53 (43.4)
T1b	16 (13.1)
T2	14 (11.5)
T3	2 (1.6)

Patients treated between 2000 and 2002, were reclassified according to the latest UICC classification <sup>9</sup>. Clinical evaluations and pathological results are summarised in Table I. Only two patients underwent radiotherapy before laryngeal laser surgery.

The proposed therapeutic protocol (transoral laser cordectomy) was discussed with the patient including risks, benefits and alternatives to the proposed treatments. Written informed consent was obtained in accordance with hospital protocols as described in our previous publication <sup>10</sup>.

All operations were performed under general anaesthesia with oro-tracheal intubation using a laser-safe endotracheal tube (Laser Flex Tracheal tube, Mallinckrodt, USA). For the laser treatment, a 25 Watt Martin CO<sub>2</sub> Laser (Martin, Germany) with a beam spot of 150 microns was

**Table II.** Patient and tumour characteristics after excision (n = 122 patients).

Characteristics	N (%)
<b>Type of Cordectomy</b>	
I	8 (6.6)
II	42 (34.4)
III	46 (37.7)
IV	6 (4.9)
V	20 (16.4)
<b>Histology</b>	
SCC	86 (71.1)
LIN 1-3	27 (22.3)
Paracheratosis	9 (6.6)
<b>Margins</b>	
Negatives	88 (72.1)
1 infiltrated margin	12 (9.8)
> 1 infiltrated margin	8 (6.6)
Close	13 (10.7)
Not evaluable	1 (0.8)
<b>Post-cordectomy Anterior Commissure Involvement</b>	
No	108 (88.5)
Yes	14 (11.5)
<b>Grading</b>	
0	42 (34.7)
1	18 (14.9)
2	54 (44.6)
3	7 (5.8)
<b>Radicalization</b>	
No	102 (83.6)
Yes (outcome = SCC)	3 (2.5)
Yes (outcome = LIN 1-3)	3 (2.5)
Yes (outcome = granulation)	14 (11.4)
<b>Duration of surgery (min)</b>	
Median (range)	112 (60-243)
<b>Total hospital stay (days)</b>	
Median (range)	3 (1-11)
<b>Post-surgery stay (days)</b>	
Median (range)	2 (0-8)

used. The parameters used were as follows: super-pulse continual mode with an output beam power set to 0.8-4.7 Watt. The cordectomies were classified by the European Laryngological Society Classification<sup>11</sup>.

Surgical techniques used in these series of patients were described in our previous publication<sup>10</sup>. The different types of cordectomies are summarized in Table II.

In all cases, including enlarged cordectomies (type III-V), specimen resections were carried out with an "en bloc"

technique. In no cases was an intra-operative biopsy was performed.

In close collaboration with the same pathologist, the pathological specimen was oriented and whole-mounted on a sponge support to prevent tissue retraction before being fixed in buffered 10% formalin. Before the specimens were fixed, every margin was stained with ink and oriented. The specimen was then serially-sectioned into 5 micron-thin sections and stained with haematoxylin and eosin and assessed for histological diagnosis. All resection margins were evaluated and the distance between tumour and specimen margins was measured.

## Results

Between January 2000 and May 2008 more than 460 TLS for early glottic cancer were performed in our Division. One hundred and twenty-two (26.5%) patients resulted to be over 70 years of age.

Definitive histopathological examination of the surgical specimens for the entire elderly patient cohort demonstrated no evidence of tumour (pT0) in 19 patients (15.6%) (calculated only in patients with a previous vocal cord biopsy positive for squamous cell carcinoma), pTis in 18 patients (14.7%), pT1a in 53 patients (43.4%), pT1b in 16 cases (13.1%), pT2 in 14 cases (11.5%) and pT3 due to invasion of the paraglottic space in 2 patients (1.6%). The disease-free margins were obtained in 88/122 patients (72.1%). Close margins were observed in 13 patients (10.7%), while one or more than one positive resection margin were found in 12 (9.8%) and 8 (6.6%) patients respectively.

In the 88/122 patients with disease-free margins, no further treatment was performed. Ten (11%) patients experienced a local recurrence. Nine of them were retreated with TLS and one with total laryngectomy. Only one patient in this group died from the laryngeal disease.

In the 33/122 patients with close-to-positive margins, 18/33 received a second transoral laser surgery, 4/33 received post-operative RT, 3/33 a second transoral laser surgery plus adjuvant RT and no further treatment in 8/33.

Regarding costs/benefits, we analyzed the duration of the treatment (cordectomies under general anaesthesia), global recovery and post surgery recovery time in the hospital. The median time of the surgical treatment, considering all different types of cordectomies and calculated from the induction of the anaesthesia to the removal of the anaesthesiology tube, was approximately 112 minutes (range 60-243 minutes). The median total recovery time was 3 days (range 1-11 days) and the median post-surgical recovery time was 2 days (range 0-8) (Table II).

We had no complications relating either to the anaesthesiological or surgical procedures. No patient needed a tracheotomy or feeding tube.

With a median follow-up of 57 months (range 5-116

months, latest census October 2008), 99 patients (81.1%) are alive without disease; one patient (0.8%) is alive with local disease, while 18 patients (14.7%) died from other causes without evidence of loco-regional disease and 4 patients (3.3%) died from the laryngeal cancer.

In 11/122 (9%) patients, we observed a second primary tumour during the follow-up period: 9/11 patients were treated for the second primary cancer and resulted to be alive at last follow-up, while 2/11 died from the second tumour (in both cases lung cancer) (Table III).

We achieved a 10-year overall survival, a tumour specific survival and a laryngeal tumour-specific survival respectively of 64.9%, 84.8 and 94.3% (Fig. 1 and Table IV).

Relapse occurred in 19/122 (15.5%) patients. Relapse was local in 17 cases and regional in 2 cases, which were treated with the following modalities:

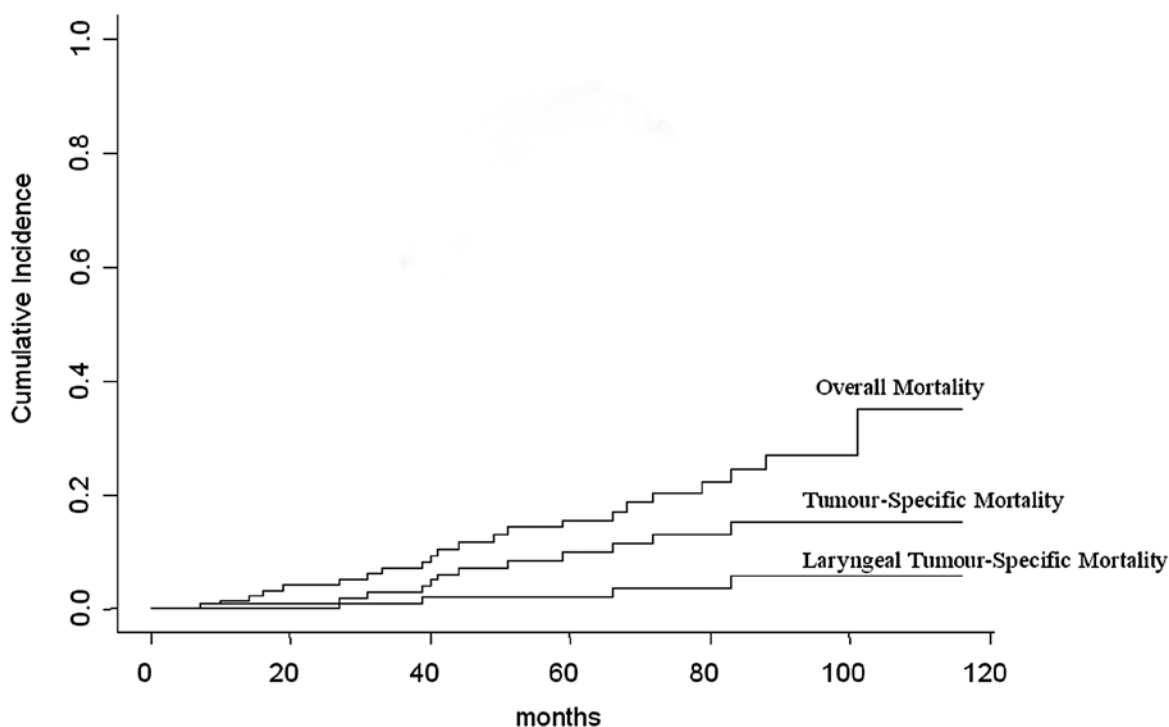
- endoscopic resection with laser in 8/19 cases (42.1%) and laser plus RT in 4/19 (21.05%);
- exclusive RT in 1/19 case (5.2%);
- exclusive CT in 1/19 case (5.2%);
- total laryngectomy in 4/19 cases (one plus adjuvant RT) (21.05%);
- selective neck dissection and RT in 1/19 cases (5.2%).

At the time of follow-up, 12/19 patients were free of dis-

**Table III.** Follow-up data (n = 122 patients).

Characteristics	N (%)
<b>Follow-up duration (months)</b>	
Total number of patients	122
Median (range)	57 (5-116)
<b>Vital status</b>	
Alive without disease	99 (81.1)
Alive with disease	1 (0.8)
Dead with disease	4 (3.3)
Dead	18 (14.7)
<b>Recurrence post-endoscopic resection</b>	
No recurrence	103 (84.4)
Local recurrence	17 (13.9)
Regional recurrence	2 (1.6)
<b>Time relapsed between surgery and recurrence (months)</b>	
Number of patients with local relapse	19
Median (range)	13 (0-84)

ease, 3/19 had died from other causes, 1/21 was alive with disease and 3/19 were dead with disease.



OM	0%	4.3%	9.4%	15.7%	22.2%	27.0%	35.1%
TSM	0%	0.8%	4.9%	9.9%	13.1%	15.2%	15.2%
LTSM	0%	0%	2.0%	2.0%	3.6%	5.7%	5.7%

**Fig. 1.** Cumulative incidence for 10-years mortality.

**Table IV.** 10-year (post-resection) survival (n = 122 patients).

	Events/patients	Univariate	
		Estimated 10-year survival	95% CI
Overall Survival	22/122	64.9%	47.1-82.7%
Tumour-specific survival	12/122	84.8%*	76.3-93.2%
Laryngeal tumour-specific survival	4/122	94.3%*	88.5-100.0%
Relapse-Free Survival	19/122	80.2%†	71.5-88.9%

\* Deaths from other causes used as competing events; † 16 deaths occurring in patients with neither local nor regional recurrence, were considered as competing events

## Discussion

In patients with early glottic cancer, literature data show that radiotherapy and conservative surgery provide comparable results in terms of local control and overall survival. Until some years ago, external beam radiotherapy with conventional fractionation represented the most common form of treatment in head and neck cancer. Compared to surgery, radiotherapy has the advantage to be a nonsurgical treatment and to be a simple, non-operator dependent technique, but the radiotherapy-related side-effects and the impact of acute and late side-effects of such a long treatment in elderly patients' quality of life are still a matter of debate. Jaime Gomez reported that the tolerance to radiation in these patients might be impaired<sup>12</sup> and Allal et al., underlined how, for this reason, treatment interruptions were more common in older patients<sup>13</sup>. Pignon et al. reported how acute and late toxicities were similar in elderly and in younger patients treated with radiotherapy for a head and neck carcinoma, even though older patients had more severe functional acute toxicity and late effects may decrease quality of life<sup>14</sup>. Olmi and co-workers compared outcomes of radiotherapy with curative intent in patients with head and neck carcinoma aged, respectively, less than and more than 70 years. They found that no differences were seen in local control and survival between the two age groups<sup>15</sup>. Also Colasanto et al. suggested that age did not correlate with local relapse rate in patients with early laryngeal cancer<sup>16</sup>. A final observation regarding radiotherapy in elderly patients may be made: radiotherapy failure patients almost always required total laryngectomy and showed an increase in post-surgical complications<sup>12-16</sup>.

Nowadays, open neck conservative surgery is considered an over-treatment for early laryngeal glottic cancer, due to low compliance to feeding and phonatory rehabilitation in elderly patients, which seriously affects the functional outcome of surgery and is frequently associated with an

increased risk of aspiration pneumonia<sup>17</sup>. Nevertheless, in older patients the open surgical strategy almost always employed is total laryngectomy which is considered an over-treatment in early laryngeal glottic cancer.

With today's ageing population, the quality of residual life highlights the importance of the treatment modalities: important secondary objectives, such as speaking voice and problem-free swallowing, are therefore requested by patients. Patient factors such as health and mental status, occupation or the desire to move independently, should guide treatment decisions: for ENT and oncologists, counselling an elderly patient on the optimal management of their problem, is sometimes quite a dilemma<sup>18</sup>. Medical conditions are critical to the assessment choice, but also recognition of special social economic needs may interfere with cancer treatment: the choice of an exclusive radiation treatment in an elderly patient, for example, must take into account compliance and the discomfort of a treatment time of 6 or more weeks, the distance to the radiation centre and difficulties for the family. In addition, the hidden costs for radiation therapy versus endoscopic excision were all greater in terms of total number of hours of work missed, total travel time, and total travel distance<sup>19</sup>.

In conclusion, our experience shows that TLS represents a feasible treatment modality in elderly patients with early stage glottic cancer providing good results in terms of disease-free survival, organ preservation and acute and late side-effects. Our group of elderly patients had no clinically relevant intra-operative or post-surgical complications and resumed normal activities the day after discharge from hospital. In our series, CO<sub>2</sub> laser removal of an early glottic cancer in elderly patients can be often considered a feasible, short hospitalisation and no-risk procedure without compromising laryngeal preservation. For patients referred to medical centres with expertise for this surgical procedure, TLS, therefore, represents a modern treatment that should be offered as an alternative to conventional radiotherapy.



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