

LARYNGOLOGY

Unravelling the risk factors that underlie laryngeal surgery in elderly

Svelare i fattori di rischio che sottendono la chirurgia laringea negli anziani

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SUMMARY

Older patients are not considered good candidates to undergo more challenging therapeutic treatments, e.g. highly invasive surgery and complex chemotherapy. However, their exclusion from standard therapeutic options is not justifiable. Herein, we reviewed 212 patients aged ≥ 70 , affected with laryngeal squamous cell carcinoma, and treated with transoral laser microsurgery or open neck (partial / total) laryngectomy with radical intent. The main aim was to compare patient outcomes to identify predictive factors that can be used by surgeons to choose the most appropriate treatment option. In our cohort, patients affected with more advanced tumour and hence treated by invasive open neck surgeries (above all TL) are more prone to develop complications and undergo fatal outcome than those with early disease treated by laser microsurgery, independently of age at surgery. In conclusion, elderly patients affected by laryngeal cancer can be treated similarly to younger patients, keeping in mind that more invasive surgeries are associated with a higher risk of developing complications. The advantages of mini-invasive surgery make it a possible first choice treatment in very old and frail patients suffering from laryngeal cancer, especially considering the recent success in treatment of some advanced stage tumours. Furthermore, comorbidities, by themselves, should not be used as exclusion criteria for subjecting an elderly patient to a different treatment that is from standard therapy.

KEY WORDS: Transoral laser microsurgery • Open partial laryngectomy • Supracricoid partial laryngectomy • Total laryngectomy • Laryngeal cancer • Elderly

RIASSUNTO

I pazienti anziani non sono generalmente considerati buoni candidati per trattamenti terapeutici impegnativi, quali ad esempio la chirurgia molto invasiva e i complessi trattamenti radio-chemioterapici. Ma la loro esclusione dalle opzioni terapeutiche standard non sembrerebbe essere del tutto giustificabile. Nel presente lavoro abbiamo esaminato 212 pazienti di età ≥ 70 anni, affetti da carcinoma squamoso della laringe, trattati chirurgicamente con diverse opzioni terapeutiche: laserchirurgia transorale o chirurgia a cielo aperto (laringectomia parziale e/o totale). L'obiettivo principale era quello di confrontare i risultati, al fine di identificare fattori predittivi utili al chirurgo per scegliere la modalità di trattamento più opportuna. Nella presente coorte, i pazienti affetti da tumore più avanzato e quindi sottoposti a interventi chirurgici a cielo aperto (soprattutto laringectomia totale) risultano maggiormente inclini a sviluppare complicanze, andando incontro a esito fatale, rispetto a quelli con malattia precoce trattati con microchirurgia laser indipendentemente dall'età al tempo dell'intervento chirurgico. In conclusione, i pazienti anziani affetti da cancro della laringe possono essere trattati come i pazienti più giovani, tenendo presente che interventi chirurgici più invasivi determinano un maggior rischio di complicanze. I vantaggi della chirurgia mininvasiva in termini di basso numero di complicanze tendono a renderla interessante come possibile trattamento di prima scelta nei pazienti molto anziani e fragili, anche in casi più avanzati. Infine le comorbidità, di per sé, non rappresentano una giustificazione per sottoporre gli anziani a trattamenti differenti da quelli standard.

PAROLE CHIAVE: Microchirurgia laser transorale • Laringectomia parziale a cielo aperto • Laringectomia parziale sopracricoidale • Laringectomia totale • Cancro della laringe • Anziani

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Introduction

The progresses in science, technology and lifestyle are allowing people to live longer and better than those who lived even 50 years ago: as a global average, life expectancy at birth has increased from 46.9 to 70.0 years in the period 1950-2015, and is expected to be 75.9 years in 2050 and

81.8 in 2100¹. The “other side of the coin”, however, resides in the concomitant increase in diagnosis of diseases that have the age as main aetiological factor (e.g. cardiovascular diseases, dementia, diabetes etc.). Among these, cancer can be considered as an archetype, inasmuch as incidence rates increase with age². As a direct consequence,

in the near future, the number of elderly with cancer will increase substantially³. In particular, amongst the different cancer histotypes, epidemiological studies foresee an increase up to 64% in diagnosis of head and neck squamous cell carcinoma (HNSCC) within the next 20 years^{4,5}. The guidelines for the treatment of HNSCC, and more specifically laryngeal SCC, require chemoradiotherapy and/or invasive surgery on the basis of tumour stage and the need to preserve organ functionality⁶. In this context, less invasive/function-sparing surgical techniques have arisen in the last decade, although they are often limited to early stage tumours or require careful selection of patients⁷⁻⁹. In this scenario, the elderly are not considered good candidates to undergo more challenging therapeutic treatments, especially highly invasive surgery and complex chemoradiotherapy¹⁰⁻¹². In addition, the management of head and neck cancer in the elderly has been historically heterogeneous, often marred by many prejudices, mainly based on both patient age and general health perceptions. In fact, aging is related to the decline of many physiological and cognitive functions, which may emphasise (and sometimes falsely require) the need to treat the elderly in a different and more limited mode than younger patients, even if no significant comorbidities are present¹³.

Nowadays, this common perception is changing: the exclusion of elderly patients from standard therapeutic options is becoming less justifiable, taking advantage potentially of all therapeutic alternatives available after a proper screening. It is therefore essential to better establish the risk to which the patient is subjected for each proposed therapeutic option, be it surgical or non surgical¹⁴.

In this 12-year multicentric retrospective study, we reviewed 212 patients aged at least 70, affected by laryngeal SCC, and treated with radical intent by 3 different types of surgical treatment: transoral laser microsurgery (TLM), open partial horizontal laryngectomy (OPHL) and total laryngectomy (TL). The population was further subgrouped into those 70-79 years old and over-80 based on age at surgery.

The main aims of this study are to evaluate the incidence of complications after laryngeal surgery and identify predictive factors for the occurrence of complications in order to provide surgeons with information to choose the most appropriate treatment option. Due to the excellent oncological results achieved in "young" adult patients with TLM, even for more advanced stage tumours¹⁵, the third purpose was to compare outcomes of TLM in elderly and frail patients, with those undergoing more invasive OPHL or TL surgeries.

Materials and methods

Patients

All patients underwent laryngeal surgery at the Hospital of Modena or at the Martini – San Luigi Gonzaga Hospitals of Turin. As previously described¹⁶, selection was

based on routinely performed clinical assessment 3 weeks before surgery to evaluate the superficial and depth extent of the tumour.

Inclusion criteria were: age at surgery ≥ 70 years, histological diagnosis of laryngeal SCC and surgical treatment with a curative purpose as single modality or as part of a multimodality approach. Comorbidities, such as diabetes mellitus, hypertension, chronic obstructive pulmonary disease, cardiac disease (i.e. chronic heart failure, arrhythmia, and coronary artery disease), and hepatic, metabolic and cerebrovascular diseases, were not considered as exclusion criteria. OPHL are interventions considered at high risk for complications related to dysfunctional sequelae.

Therefore, more stringent selection criteria were adopted to exclude patients with certain risk factors related to:

- the patient, e.g. inability to climb two flights of stairs, mental status characterised by episodes of disorientation and confusion, clinical and radiological signs of pre-existing presbyphagia and severe osteophytosis at the cervical spine;
- family situation, e.g. absence of caregivers and declared impossibility of adhering to a complete rehabilitation programme;
- tumour, e.g. advanced stage disease needing more extensive resection (classified as OPHL type I + BOT, type IIb + ARY, type III + CAU).

Characteristics of the patient cohort are summarised in Table I.

Surgery and postoperative care

After informed consent was obtained, 212 patients underwent laryngeal surgery between January 1, 2001, and

Table I. Characteristics of the 212 elderly patients undergoing laryngeal surgery according to age, sex, tumour localisation, and pathological status.

Age, y	No. of patients (%)					
Mean	75.8 \pm 4.5					
Range	70-91					
70-79	171/212 (80.7%)					
≥ 80	41/212 (19.3%)					
Sex						
Male	199/212 (93.9%)					
Female	13/212 (6.1%)					
Localisation						
Glottis	173/212 (81.6%)					
Supraglottis	39/212 (18.4%)					
Pathological Status						
	NO	N1	N2a	N2b	N2c	
pTis	12					12/212 (5.7%)
pT1	95					95/212 (44.8%)
pT2	28					28/212 (13.2%)
pT3	28	3				31/212 (14.6%)
pT4	21	14	6	4	1	46/212 (21.7%)

December 31, 2012. The choice of the surgery was based on tumour stage and comorbidities, but not considering chronological age as a discriminatory factor. Surgical procedures were transoral laser microsurgery / cordectomy in 113 patients (53.3%), open partial horizontal laryngectomy in 30 patients (14.2%), and total laryngectomy with or without pharyngectomy in 69 patients (32.5%). One hundred-twenty patients (56.6%) underwent tracheostomy. On the basis of pathological findings (pN+ and/or extracapsular spread, extralaryngeal extent, positive margins), 33 patients (15.6%) were subjected to adjuvant radiotherapy: the primary site and all draining lymph nodes were 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/2Gy; range 62-68 Gy). Furthermore, 7 patients (3.3%) received 40 mg/m² cisplatin weekly during the course of RT because of a higher risk of local recurrence.

Statistical analysis

The incidence of complications and type of surgery among different groups were evaluated by chi-square tests. The length of time from the date of diagnosis to the date of death (OS) or to the date of death for laryngeal SCC (disease-specific survival) was estimated using Kaplan-Meier curves. At the end of the study, the dates of last consultation for patients still alive were used for type-I censoring. Log-rank and Gehan-Breslow-Wilcoxon tests (for early events) were used to compare Kaplan-Meier estimates between groups (type of surgery and postoperative complications). The CHAID (chi-square automatic interaction detection) method¹⁷ was used to detect the optimal subdivision in order to maximise the differences in response within the different variables. Logistic regression was used to evaluate independent risk factors for development of perioperative and postoperative complications (within 30 days). These included age at surgery \geq 80 years, gender, presence of comorbidities, type of surgery and duration of surgery.

Kaplan-Meier curves, log-rank and Gehan-Breslow-Wilcoxon tests were performed using Graphpad Prism version 6.0c (GraphPad Software, San Diego, CA, USA), whereas CHAID analysis and multivariate logistic regression were performed with IBM® SPSS® Statistics version 22 (IBM Corp., Armonk, NY, USA), with $p < 0.05$ as the statistically significant cut-off value.

Results

Patient comorbidities

While 59 of 212 (27.8%) elderly patients who underwent laryngeal surgery did not present concomitant diseases, 86 (40.6%) patients were affected by two or more comorbidities, whereas 67 patients (31.6%) had one comorbidity. The

Table II. Distribution of patients according to the American Society of Anesthesiologists (ASA) physical status classification system.

ASA	No. of patients (%)
1	14/212 (6.6%)
2	79/212 (37.3%)
3	99/212 (46.7%)
4	20/212 (9.4%)

most frequent comorbidities were hypertension (53%), cardiac disease (17%), diabetes mellitus (17%) and chronic obstructive pulmonary disease (COPD) (12%). The severity of each comorbidity was scored and recorded according to the American Society of Anesthesiologists (ASA) physical status classification system¹⁸ (Table II).

Surgery and postoperative morbidity

The mean surgical time was 2.17 ± 1.48 h, ranging from 0.5 h to 6.5 h in patients aged 70-79 and from 0.5 h to 4.5 h in patients \geq 80 years ($p < 0.01$). Amongst treated patients, 25 patients were postoperatively transferred to the intensive care unit (ICU) where they resided for an average time between 4.4 days (70-79 years old patients) and 1.6 days (patients aged \geq 80; $p = 0.475$). The mean length of hospitalisation was 19.0 days in 70-79 patients and 12.3 in those \geq 80 ($p < 0.05$).

Perioperative or postoperative complications affected 43 of 212 patients (20.3%) of whom 36 of 171 (21.0%) in the age range 70-79 and 7 of 41 (17.1%) in \geq 80 years ($p = 0.799$).

Furthermore, stratifying patients for the type of surgery no differences between groups were observed, although open neck techniques showed a significant higher incidence of complications with respect to TLM ($p < 0.001$, Fig. 1).

In 70-79-year-old patients, 19 suffered systemic complications (mainly cardiovascular and pulmonary), 13 patients had local complications (mainly bleedings, fistulas and wound infections) and 4 developed both systemic

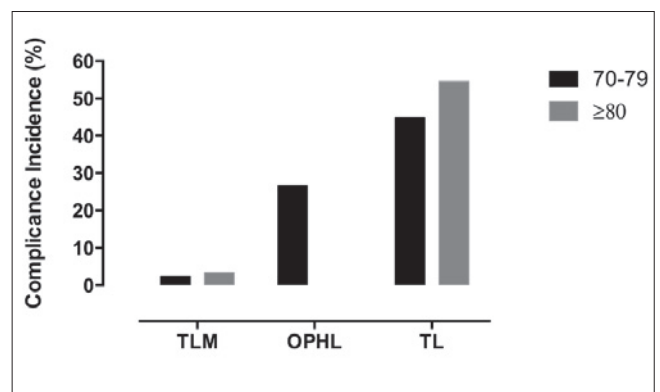


Fig. 1. Incidence of complications on patients treated by transoral laser microsurgery (TLM), open partial horizontal laryngectomy (OPHL), or total laryngectomy (TL).

Table III. Complications in patients.

Complications	Local		Number of events (%)	
			70-79	≥ 80
		Fistula	8/36 (22.2%)	0/7 (0.0%)
		Infections	4/36 (11.1%)	0/7 (0.0%)
		Haemorrhage	5/36 (13.9%)	1/7 (14.3%)
		Haematoma	0/36 (0.0%)	0/7 (0.0%)
		Necrosis	0/36 (0.0%)	0/7 (0.0%)
		Dehiscence	0/36 (0.0%)	0/7 (0.0%)
	Systemic	Pneumonia	8/36 (22.2%)	1/7 (14.3%)
		Cardiovascular*	13/36 (36.1%)	2/7 (28.6%)
		Psychiatric#	2/36 (5.6%)	7/7 (100%)
		Death	2/36 (5.6%)	1/7 (14.3%)
		Nephropathy	2/36 (5.6%)	0/7 (0.0%)
		Cerebrovascular event	0/36 (0.0%)	0/7 (0.0%)
		Hyperglycaemia	1/36 (2.8%)	0/7 (0.0%)
		Sepsis	0/36 (0.0%)	0/7 (0.0%)

* Cardiovascular complications included acute myocardial infarction, arrhythmia, and cardiac arrest # $p < 0.001$ (Fisher's exact test)

and local complications. Two patients suffered 2 systemic complications, whereas 1 patient had 2 local complications. Two patients (5.6%) died postoperatively. In the ≥ 80 year group, 7 patients developed systemic complications (mainly psychiatric): two patients had more than 1 systemic complication, whereas 1 patient also suffered a local complication (haemorrhage). One patient (14.3%) died postoperatively (Table III). Finally, 48 of 212 patients (22.6%) underwent a second surgical procedure, whereas 11 of 212 patients (5.2%) underwent a third salvage surgery.

Data from the cohort of patients undergoing OPHL are reported in Table IV.

Correlation of age, type of surgery and complications with survival

Patients were followed for a mean period of 3.05 years (range 15 days – 8.61 years). At the last follow-up, 139 of 212 patients (65.55%) were alive without disease, 25 died with disease (11.8%), 39 died for other reason than head and neck cancer (18.4%), whereas 4 were alive with disease (1.9%). The remaining 5 patients were lost to follow-up (2.35%).

At 5-years, overall survival (OS 58.0%) correlated with patient age at surgery. In fact, OS was 64.0% in 70-79 years old patients and 33.9% in those aged ≥ 80 ($p < 0.05$), with 50% mortality at 4.04 years (Fig. 2A). On the contrary, 5-year disease-specific survival (DSS, 79.7%) was not significantly affected by patient age: in fact, DSS was 83.3% and 62.8% in those 70-79 and ≥ 80 , respectively (Fig. 2B; $p = 0.062$).

Furthermore, by stratifying the data, the type of surgery or the occurrence of complications greatly affected OS (Fig. 3). In fact, patients treated by total laryngectomy

Table IV. Characteristics of patients undergoing open partial horizontal laryngectomy.

Surgery, ELS Classification		No. of patients (%)
Type IIa		11/30 (36.7%)
Type IIa + ARY		19/30 (63.3%)
Age, y		
Mean		73.2±2.2
Range		70-78
Comorbidities		No. of events (%)
	Arrhythmia	1/19 (5.3%)
	Arteriopathy	1/19 (5.3%)
	Cardiopathy	3/19 (15.8%)
	Hypertension	15/19 (78.9%)
	Ictus	1/19 (5.3%)
	Dyslipidaemia	3/19 (15.8%)
	Hypothyroidism	1/19 (5.3%)
	Diabetes	2/19 (10.5%)
	Epilepsy	1/19 (5.3%)
	HCV infection	1/19 (5.3%)
	Chronic obstructive pulmonary disease	5/19 (26.3%)
Complications		
Local	Infections	2/8 (25.0%)
	Haemorrhage	3/8 (37.5%)
Systemic	Pneumonia	1/8 (12.5%)
	Cardiovascular	5/8 (62.5%)
	Death	1/8 (12.5%)

were more prone to fatal a outcome ($p < 0.001$ and $p < 0.05$ with TLM and open partial horizontal laryngectomy, respectively), both as early event and at 5-year OS (37.2%, with 50% mortality at 4.04 years). No sig-

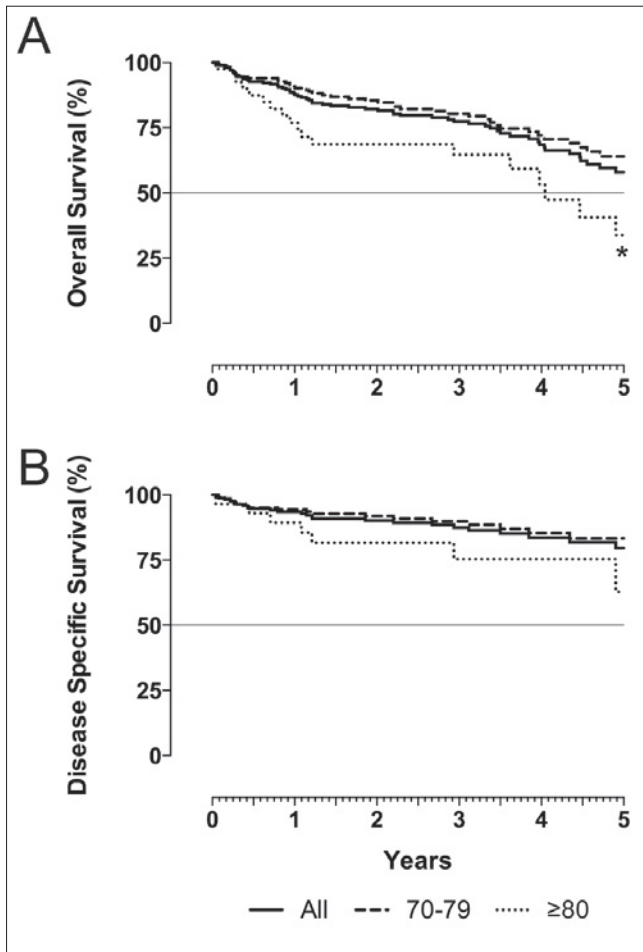


Fig. 2. Overall survival (A) and disease specific survival (B) over a 5-year period in 212 patients with laryngeal cancer. Dotted lines indicate the patient cohort according to the age at surgery. * $p < 0.05$.

nificant differences in 5-year OS were seen between patients undergoing TLM (67.7%) and open partial horizontal laryngectomy (77.9%). Similarly, 5-year OS of patients who experienced perioperative and postoperative complications was 37.5% (50% mortality at 3.50 years), which was significantly lower (as early events, also) than 62.3% (50% mortality at 6.82 years) seen in the other patients.

Age at surgery had a different impact on 5-year OS on the basis of both type of surgery and occurrence of complications (Fig. 4). In fact, patients aged 70-79 and undergoing TLM had a better 5-year OS (74.2%) than those aged ≥ 80 undergoing the same technique (48.3%, 50% mortality at 4.46 years, $p < 0.05$). Likewise, younger patients who did not experience a complication had a 5-year OS of 66.7%, which was significantly high than the older group (42.9%, 50% mortality at 4.46 years, $p < 0.05$). However, more invasive surgery as well as the presence of perioperative and postoperative complications greatly correlated with survival of ≥ 80 patients (0.0% at 5 years), whose 50% mortality was detected at 1.21 years and 0.37 years considering total laryngectomy and occurrence of complications, respectively. Patients aged 70-79 had better prognosis as an early event ($p < 0.01$) as well as 5-year OS ($p < 0.01$) for both total laryngectomy (44.8%, 50% mortality at 4.34 years) and occurrence of complications (49.7%, 50% mortality at 3.50 years).

No comparisons are available for open partial horizontal laryngectomy because all treated patients were aged 70-79 at the time of surgery.

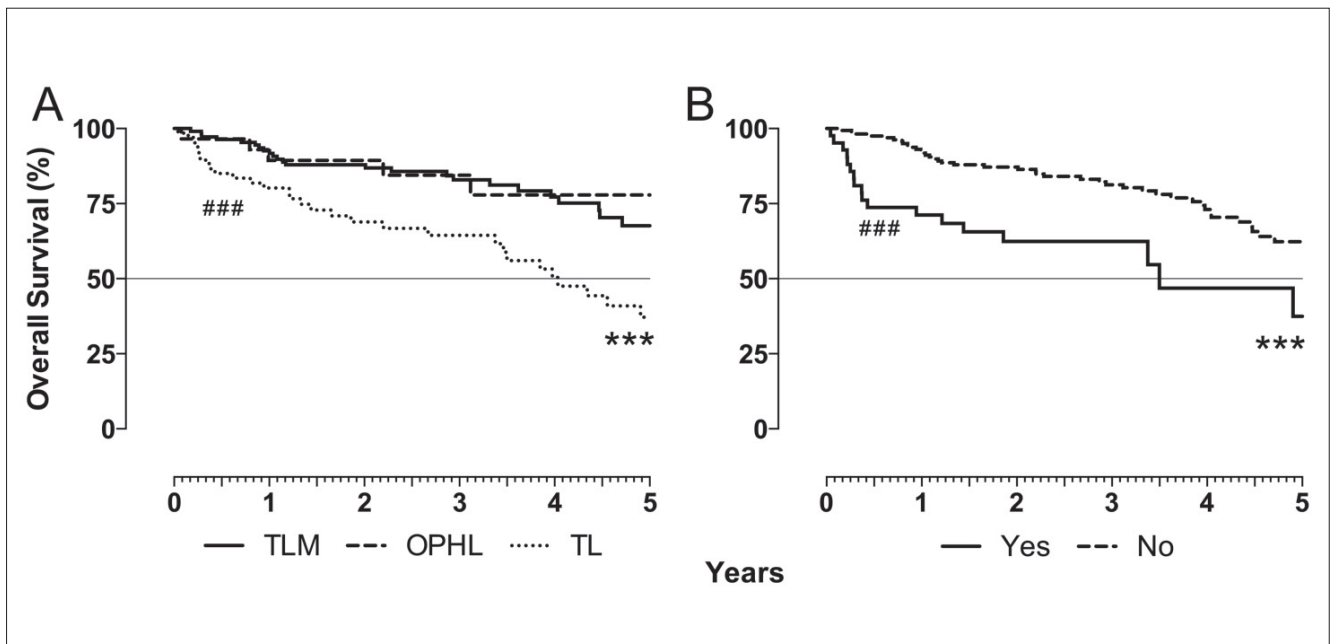


Fig. 3. Overall survival over a 5-year period in patients who underwent different surgical procedures (A) or who experienced peri- and/or post-operative complications (B). *** $p < 0.001$ (Log-Rank test); ### $p < 0.001$ (Gehan-Breslow-Wilcoxon test for early events).

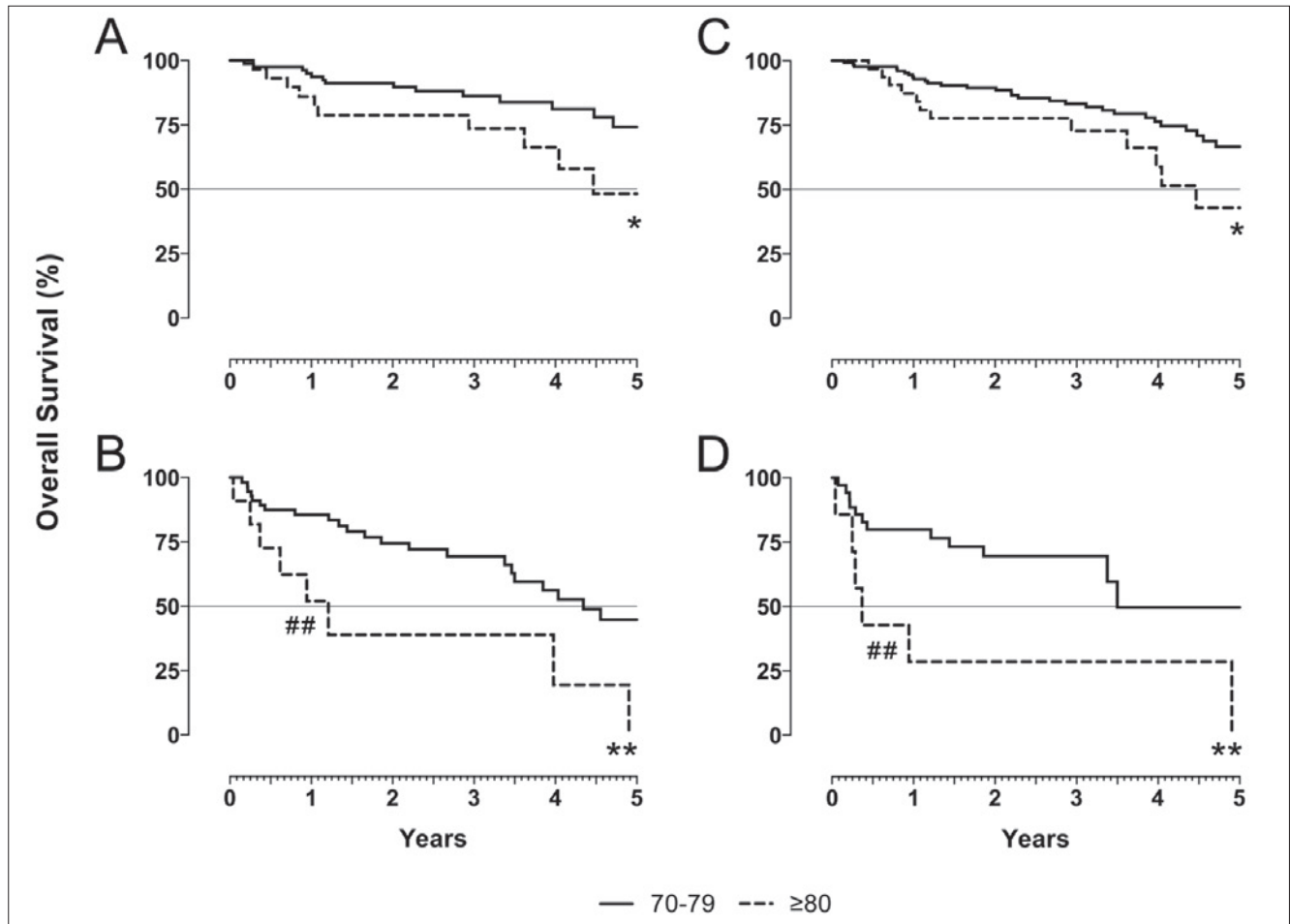


Fig. 4. Overall survival over a 5-year period in patients stratified according to the age at surgery who underwent transoral laser microsurgery (A) or total laryngectomy (B), and who did not experience (C) or otherwise show (D) complications. * $p < 0.05$, ** = $p < 0.01$ (Log-Rank test); ## $p < 0.01$ (Gehan-Breslow-Wilcoxon test for early events).

Risk analysis on the development of complications

Age ≥ 80 , sex, comorbidities and ASA physical status classification did not show statistically relevant differences considering the onset of perioperative and postoperative complications, in contrast to the duration and type of surgery. In fact, if surgery length was more than 2 hours, patients had a risk of developing complications of 37.2% compared to 10.4% for patients with surgical time ≤ 2 hours ($p < 0.001$). Likewise, patients undergoing open neck laryngectomy had a higher risk of developing complications (46.4% and 26.7% in patients treated with TL or OPHL, respectively) compared to those treated with an endoscopic technique (TLM – cordectomy, 2.7%, $p < 0.001$).

On the basis of multivariate logistical regression, we calculated the following prediction model:

$$P = \frac{1}{1 + e^{-[0.262 - 0.401(a) - 0.259(b) - 0.021(c) - 0.024(d) - 0.806(e) - 3.423(f) - 0.139(g)]}}$$

where: (a) = patient aged 70-79; (b) = woman; (c) = presence of at least 2 comorbidities; (d) = presence of 1 co-

morbidity; (e) = treatment by open partial laryngectomy; (f) = treatment by TLM; (g) time of surgery ≤ 2 h.

For total laryngectomy, the formula gave a complication rate of 46.0%-56.5% in ≥ 80 patients and 36.3%-46.5% in those aged 70-79. Similarly, the model foresaw a complication rate of 30.5%-36.7% in patients ≥ 80 treated by OPHL, while it was 22.7%-28.0% in those aged 70-79. TLM-cordectomy had very little impact on the development of complications, regardless of age. In fact, the complication risk was 2.7%-4.1% and 1.8%-2.8% for patients aged ≥ 80 and 70-79, respectively.

Discussion

Because of the ageing population, clinicians are treating older patients more often than in the past. This, and the introduction of less invasive surgical techniques, has modified the strategies that surgeons apply to treat patients suffering from laryngeal cancer¹⁹. The elderly are often treated by patient-tailored and less invasive/time-consuming procedures, making the surgeon consider

both survival expectation and quality of life after surgery. Radical surgery on older patients with advanced cancer is, however, not frequent.

The impact of oncological surgery, in particular open surgery, on the delicate equilibrium of the elderly has been the subject of various studies²⁰⁻²². Total laryngectomy separates the airways from the digestive tract, and does not expose the patient to the risk of damage for the ability to swallow, at the expense of a sudden loss of speech (usually irreversible). On the other hand, partial laryngectomy can provide the same oncological radicality while preserving the function of the larynx, even if at a lower quality, and avoiding definitive tracheostomy. The main disadvantages consist in a more restrictive selection of patients, which must be based on parameters related to the tumour, functional and cognitive abilities, absence of serious comorbidities and compliance of the patient and care-giver to an arduous rehabilitative programme, making OPHL an exception and not the rule in the management of laryngeal tumours in old (and mainly in very old) patients. However, the functional results of this surgery are long-lasting²³.

In the elderly, TLM warrants a separate discussion. It is usually employed in treatment of early stage tumour, mainly but not exclusively for glottic neoplasms²⁴⁻²⁵. However, the technique has been recently reported to be an effective surgical option even in the eradication of locally advanced stage laryngeal tumours due to the low rate of cervical node metastases²⁶. TLM, in fact, demonstrates a high level of local control, low morbidity, almost total absence of permanent tracheostomy, good compliance of patient to the operation and short hospitalisation times (less than two post-operative days).

Historically, age has been considered as either a negative prognostic factor in advanced laryngeal carcinoma²⁷ or irrelevant in the early stage for developing local relapses²⁸ and hence for disease-free survival²⁹. Furthermore, age does not have a significant impact on the long-term laryngeal function outcome after open partial laryngectomy, if the patient is selected carefully³⁰. In this context, a better understanding of the impact of age and comorbidities on post-operative outcomes in term of survival and complications may help surgeons in suggesting the best therapeutic option to patients¹⁸⁻²²⁻²⁵.

In the present study, we examined a cohort of old (aged 70-79) and very old (aged ≥ 80) patients (Table I) who underwent three different types of radical surgery. With the exclusion of OPHL that was performed only on 70-79-year-old patients due to the heavy and complex rehabilitation programme needed, the distribution of surgical techniques between groups did not reveal any statistical differences ($p = 0.139$, χ^2 test). Nonetheless, the lack of OPHL use in ≥ 80 patients did not statistically alter the reliability of comparisons (data not shown). For this reason, OPHL surgery was considered herein.

These are aggressive surgical procedures, initially resulting in severe swallowing dysfunction, most notably aspiration, but normally permitting eventual return to oral nutrition for most patients³¹.

Some independent factors influencing post-OPHL aspiration have been well studied: advanced age, extent of supraglottic resection, absence of piriform sinus repositioning and total resection of one arytenoid³².

Several authors agree that age, in itself, does not constitute an absolute contraindication, but rather a condition of increased risk. Hence, the need to be more restrictive in elderly patient selection and, if recommended, considering in advance a strategy for a simplified management of dysphagia, such as percutaneous gastrostomy²⁰⁻²³⁻³⁰⁻³².

In our experience, it is important to pay attention to: a) the mental status of elderly patients which must be quite normal in order to carry out the complex post-OPHL rehabilitation; b) the presence of motivated caregivers; c) pictures of severe osteophytosis at the cervical spine; and d) clinical and radiological signs of pre-existing presbyphagia.

As resections extended to supraglottic and subglottic sites are often associated with dysphagic sequelae, we prefer to adopt such surgery only in cases requiring resection of the glottis, saving the epiglottic tip, and enlarging to one arytenoid, if necessary¹⁰⁻³³⁻³⁵. Adopting this strategy, the complication rate was acceptable (8/30-26.6%), with only one case of fatal cardiac complication, considering a cohort characterised by a mean age of 73.2 \pm 2.2 years. Despite our analyses, patients ≥ 80 , who can be considered to be more frail than those 70-79 due to poorer 5-year overall survival (33.9% vs 64.0%, $p < 0.05$), the lack of difference in 5-year disease-specific survival (62.8% vs 83.3%, $p = 0.173$) demonstrated that the different mortality rate is not due to causes related to the cancer. In order to ascertain whether it depended merely on the reduced life expectancy of ≥ 80 patients, we analysed the impact of several covariate factors. In particular, the occurrence of perioperative and postoperative complications greatly impaired the overall survival of both 70-79 and ≥ 80 patients. Nevertheless, their occurrence was in relation to the type of surgery employed. The more invasive open neck surgeries provided a statistically higher percentage of patients with complications (up to 46.4%) than TLM (2.6%). However, stratifying the data for age at surgery, the percentage of patients who experienced complications was not statistically different between the two groups ($p = 0.694$, TLM; $p = 0.793$, TL). As a consequence, patients treated by total laryngectomy had the worst overall survival, whereas those undergoing TLM or OPHL had a similar 5-year outcomes. These results are in apparent contrast with the findings of Clayman et al. who compared the actuarial survival curve of the general population for people over 80: the global survival of elderly patients was not negatively influenced by a major operation³⁶. Indeed,

TLM was mainly adopted to treat patients affected by early carcinomas, and according to guidelines, open neck surgeries were predominantly performed on those with advanced stage tumours (Fig. 5). Accordingly, patients undergoing major operations were generally affected by more advanced pathology than those treated by less invasive techniques. As a vicious cycle, patients treated by open neck surgeries (above all TL) for a more advanced tumour are understandably more prone to develop complications and undergo fatal outcome, independently from the age at surgery. These findings are consistent with the work of Peters et al.³⁷, who carried out a large retrospective study on patients in the age range $\leq 40 - \geq 80$ affected by head and neck cancer. They concluded that age itself does not seem to be a contraindication for major head and neck surgery, although the elderly are generally affected by more comorbidities than younger patients. In this regard, it is necessary to underline how, particularly in the elderly, the selection process for curative treatment tends to exclude all patients whose comorbidities are more serious than the average for their given age. This is not a simple process, and is mostly left to the judgment of the clinician rather than an analysis of morbidity indexes. In fact, it is not justifiable to adopt a “protective” therapy for the elderly that differs from the gold standard, apart from cases in which patients present serious comorbidities. The only exception could be when heavy adjuvant therapy is necessary, since elderly patients’ compliance to lengthy treatment may be lower. In fact, as already reported, “only surgery-related variables, such as tumour stage and time of intervention, are significantly associated with surgical complications”³⁷.

Calculating the risk for each patient to undergo perioperative and postoperative complications by multivariate logistic regression, in our cohort the presence of comorbidities was not correlated with the onset of complications. In fact, the only significant covariate factor was the employment of more invasive types of surgery. The divergence with respect to the previous study could be due to the operation time evaluated, which did not include the anaesthesiologic time herein.

Conclusions

In conclusion, we infer that elderly patients affected by laryngeal cancer can be treated just as younger patients, keeping in mind that more invasive surgeries are associated with a higher risk of complications. Therefore, while for endoscopic surgery there is no reason to limit or “ponder” whether to perform surgery or not for patients of any age, open surgery on patients ≥ 80 must be thoroughly evaluated due to the higher rate of complications. The advantages of mini-invasive surgery place it as a possible first choice treatment in very old and frail patients suffering from laryngeal cancer, especially considering the

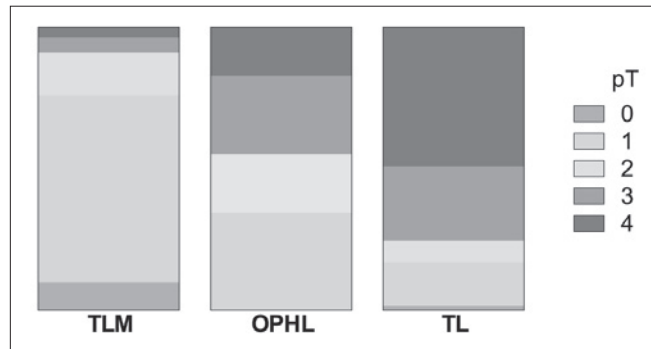


Fig. 5. Surgical procedures in relation to pT classification.

recent success in the treatment of some advanced stage tumours²⁶. Furthermore, comorbidities, in themselves, cannot justify subjecting the elderly to a treatment other than standard. Rather, the severity of these conditions defines whether the patient should be exposed to major surgical options.

Sharing and improving our knowledge in elderly patients is helpful for all physicians due to the ageing population, with the aim to improve the quality of life and overall survival in the elderly.

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