REVIEW ARTICLE

Transoral Laser Microsurgery for Locally Advanced Laryngeal Cancer

Isabel Vilaseca,* Manuel Bernal-Sprekelsen

Servicio ORL, Hospital Clinic, Facultad de Medicina, Universitat de Barcelona, Barcelona, Spain

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Keywords
Transoral laser microsurgery; Laryngeal carcinoma; Locally advanced tumours

Abstract In recent years, surgical treatment of laryngeal cancer has evolved towards transoral resections. Transoral laser microsurgery (TLM) combines microscopic control with the precise cutting and coagulation capability that laser equipment has, making it possible to remove laryngeal tumours by the transoral approach, with very good oncological and functional outcomes. In early tumours, local control with TLM has been proved to be as good as in open surgery and totally comparable to that achieved under radiation protocols, at a much lower cost. Consequently, TLM is presently considered a first line treatment in early laryngeal cancer.

These good oncological and functional results have led to an increase in TLM indications for intermediate or advanced carcinomas. In this article we review the role of TLM in the treatment of locally advanced tumours of the larynx, with special emphasis on appropriate patient selection and different technical considerations.

Although TLM is not presently considered a standard treatment for locally advanced laryngeal tumours, the outcomes published in the literature are very encouraging, with results comparable to other treatment alternatives in appropriately selected patients. Compared to external surgical procedures, TLM reduces patient morbidity, provides faster recovery and makes it possible to avoid tracheotomy in a high number of patients.

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PALABRAS CLAVE
Microcirugía transoral láser; Carcinoma de laringe; Tumores localmente avanzados

Tratamiento de los tumores laringeos localmente avanzados mediante microcirugía transoral láser

Resumen El tratamiento quirúrgico del cáncer de laringe ha evolucionado en los últimos años hacia técnicas mínimamente invasivas que permiten la resección tumoral por vía transoral. La microcirugía transoral con láser carbónico (MTL), combina la precisión y capacidad de coagulación del láser carbónico con el control microscópico, proporcionando muy buenos resultados oncológicos y funcionales. Los resultados de la MTL en tumores laringeos precoces son totalmente comparables a los de la cirugía parcial externa, con un control local igual o

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* Corresponding author.
E-mail address: ivila@clinic.ub.es (I. Vilaseca).

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superior al conseguido con la radioterapia y con un coste considerablemente inferior. Debido a ello, la MTL se considera hoy en día un tratamiento de primera elección en el tratamiento del cáncer de laringe precoz.

Los excelentes resultados de la MTL en tumores precoces han llevado paulatinamente a la ampliación de sus indicaciones a algunos tumores considerados intermedios y/o localmente avanzados. El presente artículo revisa el papel de la MTL en tumores laringeos avanzados, haciendo especial hincapié en una adecuada selección de candidatos, y facilitando detalles técnicos de la resección.

Aunque hoy en día la MTL no se considera un tratamiento estándar en los tumores laringeos localmente avanzados, los resultados publicados en la literatura son muy esperanzadores, con resultados oncológicos y funcionales totalmente equiparables a los de otras alternativas terapéuticas en pacientes adecuadamente seleccionados. Comparado con otras técnicas quirúrgicas, la MTL aporta una menor morbidad para el paciente, una recuperación funcional más rápida y la posibilidad de evitar la traqueotomía en un porcentaje muy elevado de ellos.

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Introduction

Transoral CO₂ laser microsurgery (TLM) has gradually replaced partial external surgery for the treatment of laryngeal carcinoma. The transoral approach enables an individualised surgery, planned according to the size and location of each tumour, thus preserving the maximum amount of healthy tissue. Conceptually, TLM maintains the fundamentals of open, partial surgery. Its purpose is the complete removal of the tumour with disease-free resection margins, so it is conceived as a radical treatment with curative intent.

There are some aspects which differ between TLM and external surgery. From the technical viewpoint, tumour resection in a single piece is not always possible, thus requiring the tumour to be divided into multiple blocks or fragments. Superpulse laser ablation at low power enables tissue to be sectioned with almost no carbonisation and microscopic magnification makes it possible to differentiate when cutting healthy or tumoural tissue in most cases. In areas with a more doubtful resection, TLM is supported by an intraoperative study of samples, usually obtained from the resection area.

New laser devices also enable ablation techniques at a higher power, which can achieve the removal of successive tissue layers whilst generating scarce heat lesions in depth and with good haemostasis. Tissue ablation is especially useful in large tumours or in those affecting the area of the anterior commissure and attached to the thyroid cartilage, where the mobility of the tumour specimen is highly reduced, making it very difficult to work along a perpendicular axis. However, in these cases multiple fragmentation and/or tumour ablation may hinder the final assessment of the surgical margins, most likely making them less accurate than those obtained through conventional external surgery.

From the functional standpoint, there are some characteristics that facilitate the recovery of patients treated by TLM compared to external surgery. On one hand, the possibility of resecting the larynx asymmetrically in laterised tumours allows various structures to be maintained, which would have to be sacrificed with external surgery for the sake of symmetry. Furthermore, preserving the laryngeal skeleton and infrathyroid musculature, as well as sensory structures, enables a more normalised swallowing mechanism in the immediate postoperative period. Lastly, the absence of a tracheotomy allows an elevation of the larynx upon swallowing, thus facilitating early feeding. All these features facilitate the recovery of swallowing with a lower level of aspiration, and have allowed the indications for partial surgery to be extended to include older patients and those with respiratory problems, who would have otherwise not been considered for an external partial approach.

Over the years, TLM has proven to be a very safe technique in early laryngeal tumours, reducing patient morbidity, mean length of hospital stay and avoiding prophylactic tracheostomy in a high percentage of cases. The oncological results published in early tumours are fully comparable to those obtained by partial external surgery when this is performed with adequate quality parameters, with equal or superior local control to that achieved with radiotherapy and at a considerably lower cost. As a result, TLM is currently considered as the treatment of choice for early laryngeal cancer.

The excellent results of TLM in early tumours have led to a gradual expansion of its indications to include some tumours considered as locally advanced and/or intermediate. However, at present, the scientific evidence of its usefulness in these tumours is based on short series performed by expert surgeons from few institutions and, therefore, its degree of recommendation still remains limited.

The aim of this review is to analyse the oncological and functional results of locally advanced laryngeal tumours treated by TLM.

TLM in Advanced Tumours

The literature on treatment of advanced laryngeal tumours by TLM contains some aspects which may lead to confusion. Some series analyse the results without considering tumoural sublocation, despite the fact that the behaviour of the supraglottis and glottis is different in terms of
natural history, lymphatic spread pattern, risk of distant metastasis and also in terms of organ preservation. Other studies include advanced tumours of the larynx as tumours in an advanced stage, regardless of their T classification. As a result, a certain percentage of patients present early local tumours which are labelled as advanced stages due to the presence of lymph node involvement. Finally, some authors subdivide T2 tumours into T2a (when the tumour affects 2 areas) and T2b (when there is an alteration of laryngeal mobility but no fixation), and consider the T2b group as advanced laryngeal tumours.

According to the TNM classification, locally advanced laryngeal tumours are classified as T3 or T4. Table 1 shows the characteristics of T3 and T4 laryngeal tumours according to the latest TNM classification.13

**Table 1** Characteristics of T3–T4 Laryngeal Tumours According to the Latest TNM Classification.13

<table>
<thead>
<tr>
<th>Supraglottis</th>
<th>T3</th>
<th>Tumour limited to the larynx with vocal cord fixation and/or invasion of some of the following spaces: retrocricoid, paraglottic space, minimal erosion of the thyroid cartilage (internal table) or involvement of the pre-epiglottic space</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>T4a</td>
<td>Tumour infiltrating through the thyroid cartilage and/or invading tissue beyond the larynx (trachea, cervical soft tissues, including extrinsic deep musculature of the tongue, prelaryngeal musculature, thyroid or oesophagus)</td>
</tr>
<tr>
<td></td>
<td>T4b</td>
<td>Tumour invading the prevertebral space, surrounding the carotid artery or invading mediastinal structures</td>
</tr>
<tr>
<td>Glottis</td>
<td>T3</td>
<td>Tumour limited to the larynx with vocal cord fixation and/or invasion of the paraglottic space and/or minimal erosion of the thyroid cartilage (internal table)</td>
</tr>
<tr>
<td></td>
<td>T4a</td>
<td>Tumour infiltrating through the thyroid cartilage and/or invading tissue beyond the larynx (trachea, cervical soft tissues, including extrinsic deep musculature of the tongue, prelaryngeal musculature, thyroid or oesophagus)</td>
</tr>
<tr>
<td></td>
<td>T4b</td>
<td>Tumour invading the prevertebral space, surrounding the carotid artery or invading mediastinal structures</td>
</tr>
<tr>
<td>Subglottis</td>
<td>T3</td>
<td>Tumour limited to the larynx with vocal cord fixation</td>
</tr>
<tr>
<td></td>
<td>T4a</td>
<td>Tumour infiltrating the cricoid or thyroid cartilage and/or invading tissue beyond the larynx (trachea, cervical soft tissues, including extrinsic deep musculature of the tongue, prelaryngeal musculature, thyroid or oesophagus)</td>
</tr>
<tr>
<td></td>
<td>T4b</td>
<td>Tumour invading the prevertebral space, surrounding the carotid artery or invading mediastinal structures</td>
</tr>
</tbody>
</table>

Controversial Aspects of TLM in Locally Advanced Tumours

Surgical Margin
There are some factors in TLM that determine uncertainty regarding complete resection and, therefore, may lead to a complementary treatment which threatens functional recovery. The first is difficulty in obtaining representative and assessable surgical margins throughout the entire resection. When the number of samples sent for anatomopathological study is very high, the final interpretation of these samples is complicated and may lead to confusion. Carbonisation caused by the laser, difficulty in targeting irregular fragments and retraction of the presumably healthy edge represent limitations which significantly affect the final evaluation of the margin. Hence, it is not uncommon for surgeons to obtain the final margins of arbitrarily selected areas of the tumour region, or else to systematically extend the margins of the tumour specimen by vaporisation of the region, especially in advanced tumours where the functional impact of this extension is often negligible. Additional vaporisation of the region usually pursues a double purpose: anatomical normalisation of the surgical region, which will facilitate a uniform re-epithelialisation, and systematic expansion of the margin, which tends to be overestimated erroneously in surgery performed under microscopic control. However, this extension manoeuvre results in distortion of the final condition of the margins of the surgical specimen obtained.

It is widely accepted that the presence of an affected surgical margin is associated with a high rate of local recurrence and, therefore, it is always deemed necessary to conduct an extension thereof.14,15 However, following TLM there may exist reasonable doubts as to whether the anatomopathological analysis of the specimen corresponds to the
real condition of the margin. The attitude to be adopted in this clinical situation varies according to each author. Blanch et al.\textsuperscript{14} based their decision on the anatomopathological report, the postoperative appearance of the surgical site and the surgical impression of the surgeon as per the surgical report. Margins were classified as affected, free and doubtful, with systematic expansion being recommended only in the case of affected margins and adopting a “wait and see” attitude for doubtful and free margins, as long as the surgical reports were clear regarding complete resection and the postoperative appearance of the site did not suggest tumour persistence. In their casuistry, specific survival at 5 years was 84\% among patients with clear margins, 77.9\% among patients with doubtful margins and 61.3\% among patients with affected margins, with the difference between the first 2 groups and the third being statistically significant.\textsuperscript{16}

Other authors base their decision solely on the report of the pathologist. They distinguish between positive, doubtful and negative margins, and propose surgical review in all cases of positive or doubtful margins. Based on this criterion, Jäckel et al.\textsuperscript{14} analysed the impact of margin extension in a long series of tumours throughout the upper aerodigestive tract. The prognosis of patients without extension did not differ from that of patients with negative initial margins. In cases with extension but with negative margins, the final survival was similar to that of cases with negative initial margins, but with increased risk of locoregional recurrence. Therefore, the authors suggested a closer control of these cases and even the possibility of a new extension or administration of adjuvant radiotherapy treatment. Karatzanis et al.\textsuperscript{15} also analysed the impact of repeated resections, focusing exclusively on tumours with a laryngeal location. The authors concluded that the final prognosis depended on achieving a negative margin, regardless of the number of laser sessions required to obtain it. In the case of positive margins, they found no difference between patients monitored closely and those treated with adjuvant radiotherapy.

Lastly, a third group of authors\textsuperscript{17} propose the subdivision of margins into negative, positive on the surface and positive in depth, only accepting a “wait and see” attitude in cases with superficial involvement.

There are certain manoeuvres that can be used in advanced TLM to decrease the possibility of incomplete resection. One is to seek a resection plane which is set away from the tumour boundary in those areas where a wider resection will not lead to a functional penalty. In laryngeal tumours, especially in advanced supraglottic or lateral glottic cases, this plane is often identified with the thyroid perichondrium. The blunt detachment of this perichondrium and inspection of an undamaged thyroid wing facilitate the obtention of a deep, tumour-free margin.

**Anterior Commissure**

The suitability of TLM for the treatment of tumours affecting the laryngeal anterior commissure (LAC) represents another widely discussed issue. The controversy stems from the publication of a reduced local control in this location, compared to other external, partial techniques,\textsuperscript{18} even in cases with negative margins.\textsuperscript{15} From a technical standpoint, tumours of the anterior commissure can be considered the most laborious. Their anatomical location entails greater difficulty for their exposure with rigid laryngoscopes, and their particular location does not facilitate working adequately with a laser on a perpendicular axis. Furthermore, the absence of perichondrium and early infiltration of the thyroid cartilage in this location often preclude the subperichondral blunt detachment manoeuvre, requiring an ample excision or vaporisation of the thyroid cartilage to increase the safety of the resection. The presence of a higher percentage of postoperative inflammatory granulation, as well as the possibility of in-depth tumoural persistence with extralaryngeal growth, requires these patients to be monitored by computed tomography (CT).

From a technical standpoint, it is important to differentiate between vocal cord tumours affecting the anterior commissure in a horizontal plane (T1b), from those which grow along a vertical plane, affecting the supraglottis, glottis and subglottis. Peretti et al.\textsuperscript{17} recommend treating only those tumours involving the LAC in the horizontal plane, whereas Steiner et al.\textsuperscript{19} published very good results in more advanced tumours. In a recent study, Blanch et al.\textsuperscript{20} demonstrated the importance of an extensive TLM learning curve for the management of intermediate-advanced tumours in this sublocation without affecting patient survival. In their case series, patients with tumours of the laryngeal anterior commissure (T2–T3) treated with a reduced learning curve presented worse specific survival than those treated with an extensive learning curve (71\% vs 94\%; P=0.02). The authors emphasised an aspect mentioned previously by Zeitels,\textsuperscript{21} and also recommended wide excision in a horseshoe shape, with a top-down approach which systematically included resection of the base of the epiglottis, the ventricular bands and some of the inferior preepiglottic fat. This superior wide approach does not only enable a better identification of possible in-depth infiltration, but also facilitates subsequent, fibroendoscopic control.

**Laryngeal Fixation**

Although laryngeal mobility represents a fundamental criterion in the selection of patients for conservative surgery, its clinical assessment is not always easy and has a clearly subjective component. Vocal cord hypomobility can be due to a mass effect by a large, exophytic tumour, without invasion of the paraglottic space or may be due to deep infiltration of the thyroarytenoid muscle. Exactly how much paraglottic space needs to be infiltrated in order to cause vocal cord hypomobility still remains unclear. On the contrary, when we refer to vocal cord fixation, we must determine whether or not this is accompanied by arytenoid mobility, since this is the best predictive factor of paraglottic involvement and represents a fundamental criterion for patient selection.

In a recent publication, Holsinger and Diaz\textsuperscript{22} advocated a refinement of the staging of T3 laryngeal tumours and suggested that those tumours with complete fixation of the arytenoid and vocal cord should be classified as T3b. Conversely, those tumours with scarce mobility or cord fixation, but with a functional cricoarytenoid joint should be classified as T3a. Conservative laryngeal surgery would be a possibility for the majority of such patients.

Vocal cord fixation is an independent risk factor for local recurrence in patients treated by TLM,\textsuperscript{23} with local control at 5 years ranging between 50\% and 70\%, depending on
the series. A complete approach of the superior and inferior paraglottic space requires the arytenoid to be removed. Although it is technically possible to perform total resection of the arytenoid cartilage until the cricoid membrane is exposed so the lateral cricothyroid membrane can be widely approached, in these cases it is often necessary to load the anaesthesia tube in an anterior position and support it on a rigid laryngoscope. Further exploration of the posterior commissure and posterior subglottis with laryngeal endoscopes helps to delineate the resection. However, wide excisions at this level often involve functional limitations, with secondary aspirations in the postoperative period which are difficult to treat. Therefore, unless such techniques are strictly necessary (T3a), subtotal arytenoid resection is recommended.

**Cartilage Infiltration**

Focal infiltration of the thyroid cartilage represents a criterion for the classification of a laryngeal tumour as T3. However, the TNM does not define focal infiltration clearly and, although it specifies that it refers to involvement of the thyroid internal table, it does not mention the extent of this involvement. The main clinical difficulty in these tumours with limited infiltration of the thyroid cartilage lies in their preoperative diagnosis, since the efficiency of imaging techniques (computed tomography [CT] and functional magnetic resonance imaging [fMRI]) to adequately diagnose incipient cartilage infiltration is around 60%–80%. Hence, cartilage infiltration is often an intraoperative finding by the surgeon, accompanied by the impossibility of conducting intraoperative cartilage biopsies for confirmation. In addition, we must consider that, in less calcified cartilages, there is a possibility that tumour cells circulate within the marrow. Thus, limited resection of the area of focal involvement in the inner table may be insufficient to achieve complete tumour resection. In those instances where is evidence of focal cartilage involvement, the authors recommend the removal of a cartilage window or extensive vaporisation of all the affected cartilage.

**Involvement of the Preepiglottic Space**

For a large group of authors, involvement of the preepiglottic space does not represent a limitation per se for the treatment of advanced laryngeal tumours. On the contrary, in most patients the contents of the hiothyreopiglottic space can be completely resected via a transoral approach, without implying a functional deficit in the postoperative period. However, some authors only select advanced tumours with limited invasion of pre-epiglottic tissue for transoral resection, and leave open supraglottic surgery for cases with high-volume preepiglottic involvement.

**Results of TLM in Advanced Laryngeal Tumours**

**Oncological Results**

The use of TLM in locally advanced tumours was furthered by Steiner (Göttingen, Germany), with the publication in 1993 of a first series including 82 locally advanced laryngeal tumours. Overall survival was 59% and the functional outcomes were very good. Subsequently, Iro et al. observed a local recurrence rate of 33% in 15 patients treated for supraglottic T3 and 9% in those with T4. Thus, despite the results, they discouraged the use of TLM in these tumours. In 1999, Rudert et al. reviewed a series of 34 patients with supraglottic T1–T4. Of these, 17 were locally advanced, of whom 9 were treated with palliative intent. They presented a local recurrence rate of 22% among the 9 T3 cases and 68% among the 8 T4 cases. The authors concluded that pre-epiglottic space involvement was resectable via a transoral approach. Subsequently, in 2001, the Göttingen group published the results of 167 patients with glottic T2b–T3. At 5 years, local control using laser was of 74% and 68%, respectively. Meanwhile, 50 patients with supraglottic T3 presented local control at 5 years of 86% and recurrence-free survival of 71%.

After these initial studies in Germany, other European centres have published their experience, with results comparable to those obtained using external, partial surgery. The study by Vilaseca et al. was especially relevant due to its high casuistry. The authors prospectively recorded 147 consecutive patients with T3 laryngeal carcinoma treated by TLM and analysed the prognostic factors for local recurrence and organ preservation. The local recurrence rate was higher among patients with T3 laryngeal fixation, followed by T3 cartilage infiltration and, finally, T3 pre-epiglottic involvement, with overall survival, specific survival and laryngectomy-free survival rates at 5 years of 53.1%, 70.2%, and 62.3%, respectively. More recently, the same authors have published their results with intermediate-advanced laryngeal tumours affecting the laryngeal anterior commissure in the vertical plane. Specific survival at 5 years was 79.5% for the whole series, reaching 94% among patients treated after a long learning curve.

Outside Europe, TLM has spread more slowly, especially in regard to tumours located in the larynx. In the United States, a multicentre study including laryngeal tumours in stages III-IV was published in 2007, which reported a specific survival of 58% and an organ preservation rate of 86%. However, this study included some T2 tumours and also some advanced tumours corresponded to patients in the series of Göttingen.

Tables 2 (glottis) and 3 (supraglottis) describe the oncological results among advanced laryngeal tumours treated by TLM.

**Functional Results**

One of the supposed advantages of TLM is a better and faster functional recovery of the patient, as well as a reduction in the need for prophylactic tracheotomies. These advantages, widely published in early glottic tumours, have been less extensively reported in series including supraglottic tumours, and even less in those with locally advanced laryngeal tumours.

To date, there are no randomised studies which analyse the functional results of TLM compared with supraglottic laryngectomy through an external approach, radical chemoradiotherapy or radiotherapy. Moreover, retrospective studies comparing external supraglottic surgery with the transoral alternative come from centres which primarily include within transoral treatment those tumours with limited involvement of the preepiglottic space. Therefore,
<table>
<thead>
<tr>
<th>Author</th>
<th>No.</th>
<th>TNM stage</th>
<th>Tr</th>
<th>Local control with laser 5 y. (4 y.) [3 y.] (2 y.)</th>
<th>Final local control 5 y. (4 y.) [3 y.] (2 y.)</th>
<th>Specific sv. 5 y. (4 y.) [3 y.] (2 y.)</th>
<th>Overall sv. 5 y. (4 y.) [3 y.] (2 y.)</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steiner W, 1993</td>
<td>81</td>
<td>T2–T4</td>
<td>TLM±LND±RDT</td>
<td>78%</td>
<td>-</td>
<td>-</td>
<td>59%</td>
<td>G (51)+S (30)</td>
</tr>
<tr>
<td>Ambrosch P, 2001</td>
<td>167</td>
<td>T2b–T3N0</td>
<td>TLM</td>
<td>74% (T2b), 68% (T3)</td>
<td>87% in both groups</td>
<td>62%</td>
<td>-</td>
<td>G</td>
</tr>
<tr>
<td>Davis RK, 2004</td>
<td>13</td>
<td>T2b</td>
<td>TLM+RDT</td>
<td>66%</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>G</td>
</tr>
<tr>
<td>Motta G, 2005</td>
<td>51</td>
<td>T3</td>
<td>TLM</td>
<td>65%</td>
<td>-</td>
<td>72%</td>
<td>64%</td>
<td>G</td>
</tr>
<tr>
<td>Hinni ML, 2007</td>
<td>117</td>
<td>T2–T4</td>
<td>TLM±adjuvant RDT</td>
<td>74%</td>
<td>-</td>
<td>58%</td>
<td>55%</td>
<td>G (42)+S (75)</td>
</tr>
<tr>
<td>(multicentre)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grant DG, 2007</td>
<td>10</td>
<td>T3–T4</td>
<td>TLM±adjuvant RDT</td>
<td>(68%)</td>
<td>(45%)</td>
<td>{90%}</td>
<td>(62%)</td>
<td>G</td>
</tr>
<tr>
<td>Peretti G, 2010</td>
<td>11</td>
<td>T3</td>
<td>TLM</td>
<td>71.6%</td>
<td>100%</td>
<td>-</td>
<td>-</td>
<td>G</td>
</tr>
<tr>
<td>Vilaseca I, 2001</td>
<td>51</td>
<td>T3</td>
<td>TLM</td>
<td>47.1%</td>
<td>88.2%</td>
<td>86.3%</td>
<td>73.1%</td>
<td>G</td>
</tr>
<tr>
<td>Blanch JL, 2011</td>
<td>26</td>
<td>T3</td>
<td>TLM</td>
<td>-</td>
<td>-</td>
<td>80.4%</td>
<td>-</td>
<td>LAC</td>
</tr>
</tbody>
</table>

G: glottis; LAC: laryngeal anterior commissure; LND: lymph node dissection; No.: number of patients; RDT: radiotherapy; S: supraglottis; Sv: survival; TLM: transoral laser microsurgery; Tr: treatment; y.: years.
the groups could not be homogeneous. In 2004, Cabanillas et al.\textsuperscript{36} retrospectively compared the functional outcomes of 26 patients treated with external supraglottic surgery with those of 26 patients treated by TLM, and found a significant reduction in the period for which patients had to use a nasogastric tube and also in the number of tracheotomies among the group treated with TLM. Similar results were subsequently described by Peretti et al.\textsuperscript{37} after comparing 14 supraglottic tumours treated by TLM with 14 historical controls treated by external surgery and matched by their T values. The authors analysed postoperative swallowing and voice quality with subjective methods (GRABS [grade of roughness, asthenia, breathiness, strain], VHI [voice handicap index], MDADI [MD Anderson dysphagia inventory]), as well as objective methods (acoustic analysis, endoscopic examination of swallowing and videofluoroscopy). They also assessed the hospitalisation time, duration of tube feeding or tracheostomy, and the rate of complications or aspiration pneumonia. The study revealed significant differences in favour of TLM regarding endoscopic and videofluoroscopic assessment of swallowing, hospitalisation time, duration of tube feeding and duration of tracheostomy.

A recent study analysed the long-term functional quality of a series of 39 patients with locally advanced laryngeal tumours (T3 and T4) treated by TLM and adjuvant radiotherapy or chemoradiotherapy.\textsuperscript{18} After 5 years of follow-up, 10 of the 16 living patients were assessed through quality of life questionnaires (EORTC-QLQ-C30 and C-35 and VHI), as well as objective measurements of swallowing, vocal and respiratory function. The laryngeal preservation rate was 89.7% among the total series, and 100% among patients assessed objectively. Despite this, 5 patients presented some degree of aspiration, with 3 of them requiring gastrostomy for feeding. Perceptual voice evaluation presented a mean score of 2.7 points in the RBH (roughness, breathiness, and hoarseness) scale (scoring minimal involvement as 1 and complete aphony as 4), and respiratory resistance increased in 70% of patients, being severe in 20% of cases. The authors noted that, despite some functional difficulties, the subjective quality of life could be considered good, based on the scores from the questionnaires.

Table 4 describes the functional results of TLM in locally advanced laryngeal tumours. Although functional status was not the main objective of most studies, it is noteworthy that TLM led to faster functional recovery compared to existing surgical techniques, with reduced hospital stay and a very marked decrease in the number of temporary tracheotomies. Moreover, in most publications, age and respiratory functional status have ceased to represent factors determining the exclusion of patients from undergoing partial laryngeal surgery.\textsuperscript{1, 13, 28}

### Complications of TLM in Advanced Tumours

In expert hands, TLM is considered as a safe procedure with a low complication rate. However, these data come mainly from series including small glottic tumours. Those publications including longer series of tumours in any location and their corresponding T report higher complication rates, ranging between 5% and 6%.\textsuperscript{39} The most significant complications reported are: postoperative bleeding,
Table 4: Functional Results in Patients With Advanced Laryngeal Tumours Treated With TLM.

<table>
<thead>
<tr>
<th>Author</th>
<th>No.</th>
<th>TNM stage</th>
<th>Location</th>
<th>Tr</th>
<th>Laryngeal preservation (%) 5 y. (4 y.) [3 y.] {2 y.}</th>
<th>LT-Free sv. 5 y. (4 y.) [3 y.] {2 y.}</th>
<th>Preservation of laryngeal function (%) 5 y. (4 y.) [3 y.] {2 y.}</th>
<th>Definitive gastrostomy, %</th>
<th>Definitive tracheotomy, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ambrosch P, 2001</td>
<td>167</td>
<td>T2b–T3 G</td>
<td></td>
<td>TLM±LND±RDT</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>0%</td>
<td>0.6%</td>
</tr>
<tr>
<td>Ambrosch P, 2001</td>
<td>50</td>
<td>T3 S</td>
<td>TLM+LND±RDT (neck)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>0%</td>
<td>2%</td>
</tr>
<tr>
<td>Motta G, 2004</td>
<td>18</td>
<td>T3 S</td>
<td>TLM</td>
<td>93.7%</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>0%</td>
<td>–</td>
</tr>
<tr>
<td>Davis KR, 2004</td>
<td>46</td>
<td>T2 (28) T3 (18)</td>
<td>TLM+RDT</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>3%</td>
<td>0%</td>
</tr>
<tr>
<td>Cabanillas R, 2004</td>
<td>15</td>
<td>T3 S</td>
<td>TLM+LND±RDT</td>
<td>86%</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Motta G, 2005</td>
<td>51</td>
<td>T3 G</td>
<td>TLM</td>
<td>80.5%</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>0%</td>
<td>–</td>
</tr>
<tr>
<td>Hinni ML, 2007</td>
<td>117</td>
<td>T2–T4 G (n=41)+S (n=65)</td>
<td>TLM±RDT (34%)</td>
<td>{92%}</td>
<td>{70%}</td>
<td>–</td>
<td>–</td>
<td>7% among survivors</td>
<td>3% among survivors</td>
</tr>
<tr>
<td>Grant DG, 2007</td>
<td>38</td>
<td>T1–T4 (16 T3–T4)</td>
<td>S</td>
<td>TLM±LND±RDT</td>
<td>–</td>
<td>{97%}</td>
<td>{79%}</td>
<td>13%</td>
<td>0%</td>
</tr>
<tr>
<td>Grant DG, 2007</td>
<td>10</td>
<td>T3–T4 G</td>
<td>TLM±LND±RDT</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>10%</td>
<td>10%</td>
</tr>
<tr>
<td>Olthoff A, 2009</td>
<td>39</td>
<td>Stage III–IV (T3–T4)</td>
<td>TLM±RDT±concomitant CT (6)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>89.7%</td>
<td>30% of survivors</td>
<td>10% among the entire series</td>
</tr>
<tr>
<td>Vilaseca I, 2010</td>
<td>51</td>
<td>T3 G</td>
<td>TLM±LND</td>
<td>58.9</td>
<td>51%</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Vilaseca I, 2010</td>
<td>96</td>
<td>T3 S</td>
<td>TLM±LND±RDT</td>
<td>–</td>
<td>76.6</td>
<td>74.5%</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Peretti G, 2010</td>
<td>11</td>
<td>T3 G</td>
<td>TLM</td>
<td>72.7%</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Peretti G, 2010</td>
<td>20</td>
<td>T3 S</td>
<td>TLM±LND±CT-RDT</td>
<td>88.2%</td>
<td>–</td>
<td>–</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Blanch JL, 2011</td>
<td>26</td>
<td>T3 LAC</td>
<td>TLM±LND</td>
<td>65.5%</td>
<td>–</td>
<td>–</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>

CT-RDT: chemo-radiotherapy; G: glottis; LAC: laryngeal anterior commissure; Laryngeal preservation: % of laryngeal preservation estimated including only survivors; laryngectomy-free survival: % of surviving patients (regardless of cause) with a preserved larynx; LND: lymph node dissection; No.: number of patients; RDT: radiotherapy; S: supraglottis; Sv: survival; TLM: transoral laser microsurgery; Tr: treatment; y.: years.
aspiration pneumonia, cervical emphysema, dyspnoea, local infection and cervical fistula. Of these, postoperative bleeding is the most feared complication, both due to its prevalence and to the vital risk involved for patients generally without tracheotomies.

Thus, despite being considered as a minimally invasive procedure, TLM is not without morbidity and mortality. The number of complications has been significantly correlated with tumour size, surgeon experience and tumour location,\(^4\) with \(T\) extension representing the most influential factor. Among locally advanced tumours, published mortality ranges between 0% and 3\(^%\).\(^6,31,39,41\) considered totally comparable to that of external surgery or even less than with other laryngeal preservation strategies.

Conclusions

Although TLM is not currently considered as a standard treatment for locally advanced laryngeal tumours, the results published in the literature are very encouraging, with functional and oncological outcomes which are fully comparable to those of other therapeutic alternatives in adequately selected patients. Compared with other surgical techniques, TLM offers less surgical morbidity for patients, a faster functional recovery and the possibility of avoiding a tracheostomy in a very high percentage of cases.

Nevertheless, these data originate from a small number of patients and from the experience of few centres with an advanced learning curve. Further studies are necessary in order to adequately define the surgical selection criteria for TLM and to definitively establish the role of this technique in the treatment of locally advanced laryngeal tumours.

Conflict of Interests

The authors have no conflict of interests to declare.

References