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What is This?
Comparison of Early Oncological Results of Diode Laser Surgery with Radiotherapy for Early Glottic Carcinoma

Ela Cömert, MD, PhD1, Ümit Tunçel, MD1, Ayşen Dizman, MD2, and Yıldız Yükselen Güney, MD, PhD2

Abstract

Objective. To evaluate the oncologic results of transoral endolaryngeal microscopic diode laser surgery (MDLS) and radiotherapy (RT) for T1 and T2 glottic carcinoma.

Study Design. Case series with planned chart review.

Setting. Ankara Oncology Education and Research Hospital.

Subjects and Methods. The study was conducted on a series of 140 cases of early glottic carcinoma (T1, T2) treated with MDLS or RT. The tumors were defined according to T stage and the involvement of the anterior commissure (AC).

Results. The 3-year locoregional control rate of MDLS and RT groups was 93.1% and 89.7%, respectively (P = .434). There was no difference in 3-year disease-free survival when comparing T1 and T2 tumors treated with MDLS and those treated with RT (P = .618 for T1, P = .084 for T2). There was no difference in disease-free survival when comparing AC– and AC+ tumors treated with MDLS and those treated with RT (P = .291 for AC– and P = .530 for AC+ tumors).

Conclusions. Microscopic diode laser surgery in early glottic cancer seems to be an oncologically safe procedure that has similar oncological results with RT. In T2 glottic tumors and AC involvement, the results with either treatment are less satisfactory.

Keywords

glottic carcinoma, radiotherapy, diode laser, locoregional control, survival

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Glottic cancer usually can be diagnosed at an early stage since patients with glottic carcinoma often present with hoarseness in early stages. The goal of the treatment is to cure the disease with the best achievable oncologic and functional results. Radiotherapy (RT), open surgery, and endoscopic surgery with cold steel or laser resection are the treatment modalities for early stage glottic cancer.1 The role of open surgical procedures for the management of early laryngeal cancer has greatly diminished because of the improvements in transoral laser surgery and RT.2

CO2 laser surgery was presented as one of the most accepted treatment modalities of early glottic carcinoma because of high local control rates, low morbidity, good postoperative voice quality, and low costs.3 The diode laser has recently been used for the treatment of glottic tumors. Compared with the CO2 laser, the diode laser is small, portable, versatile, and very simple to use.4 It can be used for endoscopic or microscopic surgery. The oncologic results of transoral diode laser surgery have recently been published.4,5 Local control rates and overall survival obtained in these series were comparable to those reported after RT.4,5

The aim of this study was to evaluate the oncologic results of transoral microscopic diode laser surgery (MDLS) and RT for early stage (T1 and T2) glottic carcinoma.

Methods

The study population consisted of 140 patients with early stage (T1–T2) glottic carcinoma treated at Ankara Oncology Education and Research Hospital between January 2008 and August 2012. All patients had squamous cell carcinoma of the glottic region. None had a previous history of malignant disease.

All tumors were accurately visualized through an operative microscope under general anesthesia before the initial treatment, and histological confirmation of malignancy was provided. The tumors were defined according to the 2002
American Joint Committee on Cancer–International Union against Cancer TNM system. In addition, the tumors were defined according to the involvement of the anterior commissure (AC). All patients were staged N0 after neck ultrasound examination (34.2%) or clinical examination only (65.7%). All had a chest x-ray and were free of second lung primary or metastasis.

Patients were treated with MDLS or primary RT. The choice between MDLS and RT was based on patients’ choice, the year of the disease, and pretreatment microscopic evaluation of the larynx. Microscopic diode laser surgery was introduced in our institution for the treatment of glottic carcinoma in January 2010. Before 2010, we could not apply endolaryngeal laser surgery because we had no opportunity to perform CO₂ laser surgery in our hospital. Prior to 2010, as a decision of our Head and Neck Council, most patients with early glottic carcinoma received RT. In January 2010, we changed our treatment protocol and adopted MDLS as the primary treatment for early glottic tumors. The patients were not routinely assigned to MDLS or RT in both periods (before and after 2010), but both treatment options were offered. Before 2010, RT was strongly recommended, and the patients who preferred laser surgery were referred to other institutions. After 2010, MDLS was strongly recommended, and the patients who preferred RT received RT at our institution. The single stage and short duration of the definitive treatment and the preservation of all treatment options for recurrences were the advantages of laser surgery, which were explained to the patients. The superiority of the posttreatment voice quality was the advantage of RT, which was explained to the patients. It was also pointed out that both treatments were thought to be equally effective. Tumors not suitable for laser surgery because of incomplete exposure with the microscope were treated by RT. Seventy-two patients were treated with MDLS from 2010 to 2012, and 68 patients were treated with RT between 2008 and 2012.

Radiotherapy consisted of 63 to 70 Gy from a high-voltage source as opposing lateral cervical fields. The head was routinely immobilized using a thermoplastic reproducible fixation device. Field sizes ranged from $4 \times 4$ cm to $6 \times 6$ cm covering the primary tumor site in fractions of 2 to 2.3 Gy/d, 5 days a week for 6 to 7 weeks.

For MDLS, a gallium-aluminum-arsenide diode laser (Wuhan Gigaa Optronics Technology, Wuhan, China) with the following specifications was used to excise the tumor in all cases: power 4 to 9 W and wavelength 980 nm, with a 400-μm fiber and continuous wave mode. En bloc resection was performed by cutting around the tumor and removing it in one piece. Frozen-section margins were sent to pathology to be examined from the larynx if surgical margins were considered positive. If frozen-section margins were involved by the tumor, additional tissues were removed until the margins were reported as clear. None of the patients received postoperative RT.

After both treatments, videolaryngoscopic examination was performed every 6 to 8 weeks during the year and every 3 months in the following year. Microscopic examination was performed under general anesthesia for suspicious cases.

Locoregional control was defined as the absence of failure in the larynx and in the neck. We studied and compared the disease-free intervals of MDLS and RT according to locoregional control results. The cumulative probability of surviving was analyzed according to the Kaplan-Meier method. Differences in locoregional control probability and survival among groups were analyzed by the log-rank test considering an error of 5% (ie, significant at $P < .05$). The Student $t$ test was used to compare averages and the $\chi^2$ test for comparing proportions. $P$ values $<.05$ were considered significant. The data were collected using an Excel (Microsoft, Redmond, Washington) spreadsheet. All analyses were performed by SPSS for Windows, version 15.0 (SPSS, Inc, an IBM Company, Chicago, Illinois).

The study was approved by the Institutional Review Board of the Ankara Oncology Education and Research Hospital and was therefore performed in accordance with the ethical standards in the 1964 Declaration of Helsinki.

Results

Seventy-two patients decided to have their tumor treated surgically, and 68 patients received RT. There were 129 men and 11 women. The mean age of patients in the MDLS group was 51.8 years (range, 31-75 years) and the mean age of patients in the RT group was 63.1 years (range, 30-88 years). The difference in age was statistically significant ($t$ test, $P = .033$). All patients were cigarette smokers for 22 to 45 years (mean, 32 years) in the MDLS group and 25 to 60 years (mean, 42 years) in the RT group. No significant difference between the 2 groups was observed regarding tobacco usage ($t$ test, $P = .951$). Of the 140 patients, 86 (61.4%) were T1 and 54 (38.5%) were T2. The difference between groups regarding T stage was not statistically significant ($\chi^2$ test, $P = .069$). Most patients had well to moderately differentiated carcinomas. The characteristics of the patient population are shown in Table 1.

No patient was lost to follow-up. All patients were observed for a minimum of 12 months. The mean follow-up times of MDLS and RT groups were 29.3 (range, 12-37) and 31.7 (range, 12-66) months, respectively. No significant difference between the 2 treatment groups was observed regarding the follow-up time ($t$ test, $P = .258$).

Of all patients, 12 developed a locoregional recurrence, 5 (6.9%) in the MDLS group and 7 (10.2%) in the RT group. The initial 3-year locoregional control rates for MDLS and RT groups were 93.1% and 89.7%, respectively. The difference was not statistically significant (log-rank test, $P = .434$). All regional recurrences were unilateral and treated by unilateral radical or modified radical neck dissection. Of the 68 patients treated with RT, initial local control of the primary lesions was achieved in 97.8% ($n = 46$) of T1 and 76.1% ($n = 16$) of T2 patients. Locoregional recurrence occurred 9 to 25 months after RT. All recurrences showed more advanced disease at the point of detection of the
recurrence. Surgical salvage of first recurrence with partial or total laryngectomy was achieved in all recurrences. Second recurrence (all local) occurred in 3 of these patients 10 to 15 months after the first recurrence. None of the second relapses could be salvaged with laryngectomy, and 2 of these patients died of the disease. In the RT group, the ultimate local control of T1 and T2 patients was 100% and 85.7%, respectively. After 3 years, the laryngeal preservation rate in the RT group was 94.1%.

Of the 72 patients treated with MDLS, initial control of the primary lesions was achieved in 97.4% (n = 38) for T1 and 87.8% (n = 29) for T2 patients. Locoregional recurrence occurred 10 to 15 months after MDLS. Salvage of the surgical failure by MDLS or partial laryngeal surgery was achieved in all recurrences. Two of these patients had a second local recurrence 9 to 12 months after the first recurrence, and all these patients were treated by MDLS. In the MDLS group, all patients were alive and with no evidence of disease at the time of this study, giving the ultimate control in this group of 100% for T1 and T2 patients. After 3 years, the laryngeal preservation rate in the MDLS group was 100%.

The estimated 3-year disease-free survival for MDLS and RT groups was 93.1% and 89.7%, respectively. The difference was not statistically significant (log-rank test, \( P = .434 \)) (Figure 1). The AC involvement was observed in 32 (44.4%) patients in the MDLS group and in 23 (33.8%) patients in the RT group. Survival rates of both groups according to T stage and AC status are shown in Table 2.

There was no difference in disease-free survival when comparing T1 and T2 tumors treated with MDLS and those treated with RT (log-rank test, \( P = .618 \) for T1 and \( P = .084 \) for T2 tumors). There was no difference in disease-free survival when comparing AC− and AC+ tumors treated with MDLS and those treated with RT (log-rank test, \( P = .291 \) for AC− and \( P = .530 \) for AC+) tumors. The Kaplan-Meier estimates of T2 and AC+ patients are shown in Figure 2 and Figure 3.

### Discussion

A diode (gallium-arsenide) laser is one of the most common low-energy lasers used for promoting wound healing. The basic feature of the diode laser that differentiates it from the standard CO2 laser is that the fiber of the laser passes through a straight or angled handheld fiber guidance instrument that can be held like a forceps, and the fiber directly contacts tissue. The 810-nm diode laser has been used for the treatment of early glottic tumors, and its long-term

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**Table 1. Characteristics of the Patient Population.a**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>MDLS (n = 72)</th>
<th>RT (n = 68)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>T stage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>39 (54.1)</td>
<td>47 (69.1)</td>
<td>.069</td>
</tr>
<tr>
<td>T2</td>
<td>33 (45.8)</td>
<td>21 (30.8)</td>
<td></td>
</tr>
<tr>
<td>Anterior commissure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>involvement</td>
<td>32 (44.4)</td>
<td>23 (33.8)</td>
<td></td>
</tr>
<tr>
<td>Locoregional control</td>
<td>67 (93.1)</td>
<td>61 (89.7)</td>
<td>.434</td>
</tr>
<tr>
<td>Local recurrence</td>
<td>4 (5.5)</td>
<td>4 (5.8)</td>
<td></td>
</tr>
<tr>
<td>Regional recurrence</td>
<td>—</td>
<td>1 (1.4)</td>
<td></td>
</tr>
<tr>
<td>Locoregional recurrence</td>
<td>1 (1.3)</td>
<td>2 (2.9)</td>
<td></td>
</tr>
<tr>
<td>Treatment of local recurrence</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RT</td>
<td>—</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>MDLS</td>
<td>4 (5.5)</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Partial laryngectomy</td>
<td>1 (1.3)</td>
<td>2 (2.9)</td>
<td></td>
</tr>
<tr>
<td>Total laryngectomy</td>
<td>—</td>
<td>4 (5.8)</td>
<td></td>
</tr>
<tr>
<td>Second recurrence</td>
<td>2 (2.7)</td>
<td>3 (4.4)</td>
<td></td>
</tr>
<tr>
<td>Treatment of second recurrence</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RT</td>
<td>—</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>MDLS</td>
<td>2 (2.7)</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Total laryngectomy</td>
<td>—</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Palliative treatment</td>
<td>—</td>
<td>3 (4.4)</td>
<td></td>
</tr>
<tr>
<td>Ultimate larynx</td>
<td>100</td>
<td>94.1</td>
<td></td>
</tr>
<tr>
<td>preservation rate, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follow-up, mean (range), mo</td>
<td>29.3 (12-37)</td>
<td>31.7 (12-66)</td>
<td>.258</td>
</tr>
</tbody>
</table>

Abbreviations: MDLS, microscopic diode laser surgery; RT, radiotherapy; —, no patients.

*Values are presented as number (percentage) unless otherwise indicated.

**Table 2. Main Oncologic Results in Study Patients.**

<table>
<thead>
<tr>
<th>T and AC Status</th>
<th>MDLS Group, %</th>
<th>RT Group, %</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>97.4</td>
<td>97.9</td>
<td>.618</td>
</tr>
<tr>
<td>T2</td>
<td>87.9</td>
<td>71.4</td>
<td>.084</td>
</tr>
<tr>
<td>AC−</td>
<td>97.5</td>
<td>93.3</td>
<td>.291</td>
</tr>
<tr>
<td>AC+</td>
<td>87.5</td>
<td>82.6</td>
<td>.530</td>
</tr>
</tbody>
</table>

Abbreviations: AC, anterior commissure; MDLS, microscopic endolaryngeal diode laser surgery; RT, radiotherapy.

and 87.8% (n = 29) for T2 patients. Locoregional recurrence occurred 10 to 15 months after MDLS. Salvage of the surgical failure by MDLS or partial laryngeal surgery was achieved in all recurrences. Two of these patients had a second local recurrence 9 to 12 months after the first recurrence, and all these patients were treated by MDLS. In the MDLS group, all patients were alive and with no evidence of disease at the time of this study, giving the ultimate control in this group of 100% for T1 and T2 patients. After 3 years, the laryngeal preservation rate in the MDLS group was 100%.

The estimated 3-year disease-free survival for MDLS and RT groups was 93.1% and 89.7%, respectively. The difference was not statistically significant (log-rank test, \( P = .434 \)) (Figure 1). The AC involvement was observed in 32 (44.4%) patients in the MDLS group and in 23 (33.8%) patients in the RT group. Survival rates of both groups according to T stage and AC status are shown in Table 2. There was no difference in disease-free survival when comparing T1 and T2 tumors treated with MDLS and those treated with RT (log-rank test, \( P = .618 \) for T1 and \( P = .084 \) for T2 tumors). There was no difference in disease-free survival when comparing AC− and AC+ tumors treated with MDLS and those treated with RT (log-rank test, \( P = .291 \) for AC− and \( P = .530 \) for AC+) tumors. The Kaplan-Meier estimates of T2 and AC+ patients are shown in Figure 2 and Figure 3.

**Figure 1.** Disease-free survival rates for endolaryngeal microscopic diode laser surgery (MDLS) and radiotherapy (RT) groups 3 years after treatment.
oncologic results were established in 2008. It was not well accepted worldwide, and most institutions continued using the CO2 laser. The 980-nm diode laser is a new technology, and it recently has been introduced for the treatment of early glottic tumors. The main difference between these 2 diode laser types is their effect on healing. It has been demonstrated that the 980-nm diode laser therapy accelerates the wound-healing process by changing the expression of PDGF and bFGF genes responsible for the stimulation of cell proliferation and fibroblast growth. This special feature of the 980-nm diode laser allows it to become a strong alternative to the CO2 laser.

The choice between RT and MDLS in our study was not a random choice and was based on 3 factors: patients’ choice, the year of the disease, and pretreatment microscopic evaluation of the larynx. At the Ankara Oncology Education and Research Hospital, a tertiary referral hospital, MDLS has been increasingly applied as the treatment of first choice for T1-T2 glottic laryngeal carcinoma since 2010. Before 2010, as a decision of our Head and Neck Council, RT used to be the treatment of first choice. Between 2008 and 2010, approximately one-third of the patients referred to other institutions for CO2 laser surgery and two-thirds of the patients received RT at our institution. In 2010, we updated our decision on the treatment of T1-T2 glottic tumors in our Head and Neck Council and recommended MDLS as the initial treatment. This shift in treatment of first choice was due to the development of more advanced laser techniques and our opportunity to perform MDLS at our institution. We also observed a 2-fold increase in the number of patients who were referred to our institution after 2010 because of the popularity of MDLS. Currently, since 2010, RT is recommended for patients who do not accept MDLS or for tumors that are not suitable for laser surgery because of incomplete exposure. Between 2010 and 2012, approximately two-thirds of the patients underwent MDLS and one-third received RT. The estimated depth of infiltration of the tumor did not affect the choice of treatment.

In most previous studies comparing CO2 laser surgery and RT, laser surgery was preserved for the more superficial tumors, while RT was applied for the larger and deeper infiltrating tumors. Previous studies also indicated that the cure rate of CO2 laser surgery was equal to RT for T1 glottic tumors. Deep tumor infiltration or AC involvement requires cordectomy types IV to V according to the European Laryngological Society classification, and impaired voice quality is the expected result of type IV to V cordectomy. For these tumors, RT is often preferred as the primary treatment because the quality of voice is generally perceived to be better. In our series, many patients with a T2 tumor or AC involvement preferred MDLS. According to our results, there was no significant difference in disease-free survival rates when comparing T2 and AC+ patients treated with MDLS and those treated with RT. In T2 glottic tumors and AC involvement, the results with either treatment modality are less satisfactory.

Like CO2 laser, main advantages of MDLS include short hospital stay (1-3 days postoperatively) and the preservation of all treatment options, including repeated laser surgery, radiotherapy, and open surgery for recurrences. Since we did not have CO2 laser in our clinic, we did not have the chance to compare our results of the CO2 laser and MDLS. Preliminary results of MDLS were similar to CO2 laser surgery. Initial local control rates at 5 years with CO2 laser excision were reported as 82% to 90% for T1 and 70% to 91% for T2 glottic tumors. In our series, the initial locoregional control rate at 3 years with MDLS was 97.4% for T1 and 89.7% for T2 tumors. The disease-specific 5-year survival for the CO2 laser was reported as 96% for T1 tumors and 83% for T2 tumors. We analyzed the disease-free survival rate of MDLS and found similar results with the CO2 laser. The larynx preservation rate of MDLS was also similar to the CO2 laser.
Management after irradiation failure still remains a controversial topic. An increased complication rate is usually anticipated when salvage surgery is performed after irradiation failure. The increased duration of tracheotomy, significant postoperative edema, and delayed wound healing were reported as the complications of salvage surgery.\textsuperscript{18} Most recurrences in irradiated patients show more advanced disease at the point of detection of the recurrence and therefore are treated with total laryngectomy.\textsuperscript{16,19} The larynx preservation rate of RT was reported as 77% to 83% for early glottic tumors.\textsuperscript{16,20} Previous reports advocated that ultimate larynx preservation was significantly higher in patients initially treated with laser surgery compared with those initially treated with RT.\textsuperscript{11} The diseasespecific 5-year survival for RT was reported as 93% for T1 tumors and 88% for T2 tumors, and the initial local control rate of RT was reported as 67% to 94% for T1-T2 tumors.\textsuperscript{16,17} Our results of RT concur with the current literature.

To our knowledge, this is the first report comparing MDLS and RT for early glottic carcinoma. The main drawback of our study is the relatively short follow-up of the patients. We could not present oncologic results of MDLS at 5 years, since MDLS was only introduced in our institution in 2010. A 3-year follow-up is considered sufficient because at least 90% of the recurrences, either local or regional, appear within the first 2 years.\textsuperscript{21} Radiotherapy has been established as an efficient treatment for early glottic carcinoma, whereas MDLS is a new treatment modality for laryngeal tumors. Although the oncologic results of MDLS do require more follow-up, at this stage, they are promising. In our study, we found no statistically significant differences in the 3-year locoregional control and disease-free survival rates between patients who underwent MDLS and patients who received RT. The larynx preservation rate was better in the MDLS group (100% vs 94.1% in the RT group).

Microscopic diode laser surgery in early glottic cancer seems to be an oncologically safe procedure that has similar 3-year disease-free survival and locoregional recurrence rates to RT. Further studies are needed to evaluate the efficiency and long-term results of MDLS.

**Author Contributions**

Ela Cömert, analyzed data, revised article, wrote article, study design; Umit Tunçel, analyzed data, revised article, wrote article, study design; Ayşen Dizman, analyzed data, revised article, wrote article, study design; Yıldız Yükselen Güney, analyzed data, revised article, wrote article, study design.

**Disclosures**

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**References**


