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Oncologic Outcomes of KTP Laser Surgery Versus Radiation for T1 Glottic Carcinoma

Jamal Ahmed, MD; Ahmed Sherif Gabr Ibrahim, MD; Laura M. Freedman, MD; David E. Rosow, MD

Objectives/Hypothesis: To characterize outcomes for patients who underwent transoral microsurgery with potassium titanyl phosphate (KTP) laser resection of early glottic cancers and to compare outcomes with patients who received external beam radiation therapy.

Study Design: Retrospective cohort study.

Methods: The history of patients with T1 glottic carcinoma treated with curative primary radiation or transoral KTP laser resection was reviewed. Oncologic outcomes for both radiation and surgery cohorts including disease-free and overall survival were calculated.

Results: Eighty-seven patients met inclusion criteria from 2011 to 2016; 47 patients (54%) received primary KTP laser ablation, and 40 patients (46%) received primary external beam radiotherapy. The average length of follow-up was 924 ± 529 days in the KTP laser group and 994 ± 603 days in the radiation group (P = .26). There were no significant differences between the two treatment groups in terms of medical or demographic variables. There were six recurrences in the KTP laser group (13%), versus six in the radiotherapy group (15%) (P = .77). The laryngeal preservation rate for the cohort of patients who initially received KTP laser treatment was 46 out of 47 patients (98%). Of the cohort that received primary radiation therapy, the laryngeal preservation rate was 36 out of 40 patients (90%, P = .18). Disease-free and overall survival were 88% and 98% in the KTP laser cohort and 85% and 95% in the radiation cohort (P = .78, P = .56), respectively.

Conclusions: KTP laser ablation is a modality equivalent to primary radiation therapy in oncologic outcomes for T1 glottic squamous cell carcinoma.

Key Words: Laryngeal cancer, early glottic cancer, laser, radiation therapy, outcomes.

Level of Evidence: 4.

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INTRODUCTION

Laryngeal carcinoma is one of the most common upper aerodigestive tract malignancies, and glottic carcinoma is the most common subtype. The incidence of laryngeal carcinoma and deaths from carcinoma is decreasing, likely due to the decreased prevalence of tobacco use. The vast majority of these laryngeal cancers are squamous cell carcinomas in patients with a history of tobacco smoking. Many patients present with voice changes or hoarseness in the earliest stages of carcinogenesis, which allows for expeditious evaluation and treatment of many tumors while they are still relatively small. There are multiple options for treating early-stage glottic carcinoma, and these consist of open surgery, transoral laser microsurgery, or radiation. For patients who fail radiation, surgical salvage remains an option, ranging from focal ablations to total laryngectomy.

At present, transoral laser microsurgery (TLM) is the mainstay of surgical therapy for early glottic carcinoma. The benefits of laser resection include improved hemostasis, precise control of depth of ablation, and the ability to repeat therapy while avoiding open neck surgery. In addition, primary utilization of TLM allows saving radiation therapy as a valuable salvage therapeutic. Although TLM has historically been performed with a carbon dioxide (CO₂) laser, there is a small but growing literature base for the use of potassium titanyl phosphate (KTP) laser for glottic carcinoma.

The KTP laser is primarily absorbed by red pigment, such as hemoglobin, which makes it an excellent instrument for selectively vaporizing tissues that are highly vascularized, a process known as selective photoangiolyis. Taking advantage of this property of the KTP laser can allow for effective oncologic resection while minimizing the energy delivered, and therefore causing less collateral tissue damage. Given the proven link between angiogenesis and tumor growth, it is understandable that the KTP laser would be an attractive instrument for cancer ablation, and early research has shown acceptable oncologic and voice outcomes similar to those seen with the CO₂ laser.

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undertaken to prove the hypothesis that oncologic outcomes will not be significantly different in patients receiving primary radiation therapy or primary transoral KTP laser resection for T1 glottic carcinomas at a single academic institution.

MATERIALS AND METHODS

Patient Selection

Institutional review board approval was granted for a retrospective chart review of patients aged 18 years and older treated between January 2011 and January 2016 at a single academic tertiary referral center for T1a or T1b squamous cell carcinoma of the vocal folds. Treatment for all patients consisted of either primary external beam radiation therapy (EBRT) or KTP-TLM. A choice of either treatment was offered to all patients and was made according to several factors, including patient preference, perceived difficulty of operative microlaryngoscopic exposure, and ability to tolerate general anesthesia. Patients with a prior history of glottic cancer, or any other head and neck malignancy, were excluded. Demographic and clinical data were extracted via chart review and analyzed. Objective vocal parameters were obtained from the surgical group including F0 (fundamental frequency), jitter (a measure of frequency variation), shimmer (a measure of amplitude variation), and noise-harmonic ratio. Subjective voice assessment was obtained through pre- and postoperative Voice Handicap Index (VHI-10) scores. Oncologic outcomes for both radiation and surgery cohorts including disease-free survival and overall survival were calculated.

Statistical Analysis

Contingency tables were used to compare categorical variables in the KTP-TLM group versus the EBRT group using the Fisher exact test and \( \chi^2 \) test for trend. Continuous variables were analyzed using Mann-Whitney tests and Student t tests. Oncologic outcomes (disease-free survival and overall survival) were determined using Kaplan-Meier plots for each cohort and both log-rank (Mantel-Cox) test and Gehan-Breslow-Wilcoxon tests. Pre- and postoperative voice parameters were examined using Wilcoxon matched-pairs signed rank test. Prism GraphPad software (GraphPad Software, Inc., La Jolla, CA) was used to analyze data. Statistical significance was determined as \( P < .05 \).

RESULTS

A total of 137 patients were seen at our institution for a diagnosis of T1 glottic cancer over the study period. Of these, 50 patients were excluded from analysis due to being recurrent cases, being upstaged at surgery, having a history of other head and neck malignancy, declining treatment, or having treatment elsewhere. This resulted in 87 patients who met inclusion criteria, 47 of whom received primary KTP laser ablation and 40 who received primary EBRT. This represented all patients who underwent primary treatment for T1 glottic carcinoma at our institution over the time period studied. Average length of follow-up was 924 ± 529 days in the KTP laser group and 994 ± 603 days in the radiation group (\( P = .26 \)). There were no significant differences between the two treatment groups in all demographic variables and comorbidities studied, including average age, gender, average body mass index, alcohol/tobacco use, diabetes, coronary artery disease, chronic obstructive pulmonary disease, gastroesophageal reflux disease, or stroke (data not shown). Both groups had similar proportions of patients present with hoarseness, dysphagia, or shortness of breath; the vast majority of patients presented with hoarseness. In addition, both groups had similar proportions of patients with T1a and T1b disease, as well as the presence or absence of anterior commissure involvement (Table I).

For the six patients who recurred after KTP-TLM, all were offered a choice of revision surgery versus radiation. Three patients lived a long distance from our institution and chose to undergo radiation therapy closer to home. Two additional patients chose radiation at our institution, for a total of five patients who received successful salvage radiation therapy. The sixth patient underwent a total laryngectomy for a large recurrence but died due to progression of disease. The final laryngeal preservation rate for the cohort of patients who initially underwent primary KTP laser resection was 46 out of 47 patients (98%), with an average follow-up of approximately 31 months.

In the primary radiation group, 29 patients (73%) received 63 Gy, one (3%) received 64 Gy, six (15%) received 65.25 Gy, three (8%) received 66 Gy, and one (3%) received 68 Gy. There were six recurrences in the radiotherapy group (Table II). Of these patients, four underwent total laryngectomy for the recurrence, and two of these patients died of disease. One patient maintained local control but recurred in the neck; this was successfully treated with neck dissection. The remaining patient underwent two courses of additional KTP laser ablation for two recurrences. Of the cohort that received primary radiation therapy, the laryngeal preservation rate was 36 out of 40 patients (90%, \( P = .18 \)). For the patients who received primary radiation therapy and then recurred, the final laryngeal preservation rate was 33%. For patients who

### TABLE I.

<table>
<thead>
<tr>
<th></th>
<th>KTP-TLM</th>
<th>EBRT</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>47</td>
<td>40</td>
<td>–</td>
</tr>
<tr>
<td>T1a (77%)</td>
<td>36</td>
<td>28</td>
<td>.63</td>
</tr>
<tr>
<td>T1b (23%)</td>
<td>11</td>
<td>12</td>
<td>.63</td>
</tr>
<tr>
<td>AC involved</td>
<td>12 (26%)</td>
<td>15 (38%)</td>
<td>.25</td>
</tr>
<tr>
<td>AC spared</td>
<td>35 (74%)</td>
<td>25 (62%)</td>
<td>.25</td>
</tr>
</tbody>
</table>

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recovered after KTP laser treatment, the final laryngeal preservation rate was 83% ($P = .24$).

The average number of days until recurrence was diagnosed was 450 ± 206 days in the KTP-TLM group and 514 ± 333 days in the EBRT group ($P = .27$). Disease-free and overall survival rates, respectively, were 87% and 98% in the KTP-TLM cohort and 85% and 95%, respectively, in the EBRT cohort ($P = .78$, $P = .56$) (Figs. 1 and 2). There were no statistically different proportions of patients with T1b disease or anterior commissure involvement in the KTP laser group versus the radiation group. The presence of T1b disease or anterior commissure involvement had no statistically significant effect on recurrence rate ($P = .63$, $P = .25$).

Twenty-one patients who received KTP laser ablation had objective voice assessments both preoperatively and postoperatively (Fig. 3). These demonstrated a significant decrease in shimmer, jitter, and noise-to-harmonic ratio ($P < .05$). There was no significant change in F0. Eleven patients had received both pre- and postoperative VHI-10 questionnaires. These demonstrated a statistically significant decrease in the VHI-10, indicating perceived voice improvement ($P = .002$). Although a significant proportion of patients were missing either pre- or postoperative objective and subjective assessments, those who did possess both were compared, using each patient as his or her own control.

**DISCUSSION**

This study aimed to characterize the clinical outcomes between similar cohorts of patients with T1 glottic carcinoma treated with KTP-TLM or with EBRT. Overall, T1 glottic carcinoma has a high rate of disease-free and overall survival. Demographics and comorbidities including age, smoking burden, and cardiopulmonary diseases were compared between the KTP-TLM and EBRT groups. No significant differences were demonstrated. In addition, both groups were treated at the same tertiary referral hospital system, with all surgeries performed by a single surgeon.

The relatively sparse lymphatics of the glottis permit the safe employment of close margins with good oncologic and functional outcomes (Fig. 4). The use of KTP angiolytic laser in this study generated acceptable oncologic outcomes as measured by disease-free and overall survival. Similarly, the rate of laryngeal preservation in our study, as measured by a clinical course spared from total laryngectomy, is high. These rates are similar to those seen in other published studies examining CO2 laser TLM for early glottic carcinoma, which are over 90% for both disease-free and overall survival. To date, there have only been two other groups that have published on the oncological efficacy of KTP-TLM versus EBRT, and our results confirm their findings as well. However, this is the first study that directly compares the results of KTP-TLM to EBRT within a single institution.

It is notable that five of six patients who failed KTP-TLM treatment opted for radiation treatment instead of repeat surgery, but this was likely due to patient-specific preferences. Both subjective and objective vocal parameters showed significant improvement after treatment, which is consistent with other studies examining CO2 laser TLM. However, our study only collected voice data in a subset of surgical patients, and very few radiation patients, such that statistical comparison was not possible.

Radiation therapy was also a highly successful treatment modality, with similar disease-free and overall survival to the KTP-TLM group at 3 years in this study. Patients received between 63 and 68 Gy, with the majority receiving 63 Gy. Patients who failed radiation had doses throughout this range, with three receiving 63 Gy and one each receiving 65.25, 66, and 68 Gy. Although there was minor variation in the dosing of radiation, the same group of radiation oncologists administered the therapy, and this produced overall similar therapeutic approaches for each patient. Voice outcomes could not be examined in the EBRT group due to a lack of data. The...
presence of acute or late toxicity was not examined in this study. The presence of severe (grade III) toxicity is rare in early-stage glottic carcinoma treated with definitive radiotherapy alone.\textsuperscript{14} Mild and moderate (grade I and II, respectively) toxicity is seen in a majority of radiotherapy patients and is typical during and immediately following treatment.\textsuperscript{15,16} Grade I laryngeal radio-toxicity includes hoarseness and slight arytenoid edema, whereas grade II includes moderate arytenoid edema and chondritis, as well as skin erythema and esophagitis.\textsuperscript{17} A 2017 meta-analysis by Mo et al. of 11 studies comparing functional and oncologic outcomes of TLM versus radiation therapy found significantly improved laryngeal preservation rate and overall survival in the TLM group.\textsuperscript{18} However, this analysis did not take into account clinical and demographic factors of each patient group, and the local control rate was not significantly different between the two groups. A study of 75 patients
Objective outcomes between TLM and EBRT. A meta-analysis of voice outcomes by Greulich et al. showed similar subjective and objective outcomes between TLM and EBRT.

One of the ongoing goals in management of laryngeal cancer is stratification of patients into high- and low-risk groups. Low-risk patients may be candidates for more focused treatment, such as KTP laser ablation, to maintain oncologic efficacy while reducing side effects and preserving voice and swallowing, whereas higher-intensity regional treatment, such as radiation, can be selected to prevent tumor recurrence in high-risk patients. Despite this potential utility, there are currently no consensus markers for risk stratification in early glottic cancer.

The link between tobacco use and squamous cell carcinoma of the aerodigestive tract has been firmly established, but in this study neither the presence of active smoking nor history of increased years of smoking was shown to affect response rates to EBRT or KTP-TLM. Interestingly, one study found a subgroup of patients with a more papillary type of vocal fold carcinoma was identified with no tobacco use history, and it has been speculated this may be due to human papillomavirus infection.

Anterior commissure involvement has been shown to be a risk factor for recurrence of early glottic carcinomas, however, our study did not see a significant increase in recurrence risk with anterior commissure involvement in either group.

**Limitations of the Study**

As this is a retrospective study, we cannot eliminate the effect of selection bias for patients who received radiation versus those who received KTP-TLM. Healthier patients with smaller tumors could be deemed better surgical candidates, whereas radiation could be reserved for larger, more diffuse tumors that would have a poorer prognosis. On the other hand, some patients can be deemed too sick to undergo a course of primary radiation and are offered surgery instead. Bias was also partially mitigated by the fact that patients were ultimately offered a choice between both treatments. The small sample size and the difference in follow-up lengths may also have prevented detecting true differences between the two treatment groups. There was a significant amount of missing data for voice outcomes, including for the vast majority of the patients treated with radiation, which precluded our ability to compare functional outcomes between the two groups.

**CONCLUSION**

KTP transoral microsurgical ablation of T1 glottic squamous cell carcinoma is a modality that is equally efficacious as primary radiation therapy and one which provides adequate oncologic outcomes. Preliminary voice data suggest that KTP-TLM affords acceptable functional outcomes as well, but this will need to be assessed in a prospective trial comparing these results to patients receiving EBRT.

**BIBLIOGRAPHY**