Received: 31 October 2020 | Revised: 6 February 2021 | Accepted: 17 April 2021

DOI: 10.1002/lio2.572

ORIGINAL RESEARCH

Laryngoscope Investigative Otolaryngology

Flexible fiber-based CO_2 laser vs monopolar cautery for resection of oral cavity lesions: A single center randomized controlled trial assessing pain and quality of life following surgery

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Funding information
National Cancer Institute, Grant/Award Number: P30 CA008748; Omniguide Surgical

Abstract

Importance: This study reports the impact of laser surgery on quality of life in patients with oral cavity lesions.

Objective: To compare postoperative pain and quality of life in patients treated with flexible fiberoptic CO_2 laser vs electrocautery in patients with oral cavity precancerous lesions and early stage cancers.

Design: Randomized controlled trial.

Setting: Single center.

Participants: Patients with premalignant oral cavity lesions and early stage oral cancer.

Intervention: Patients were randomized to have surgical resection using either flexible fiber carbon dioxide laser (Laser) or electrocautery (EC). The patients were then followed over a period of 28 days to assess for outcomes including pain, quality of life, performance status, return to work, and return to diet. Quality of life was measured by the University of Washington Quality of Life (UWQOL) questionnaire and the performance status score (PSS).

Main outcome measure: The primary endpoint for this study was the numerical pain rating on postoperative day (POD) 7.

Results: Sixty-two patients were randomized (32 laser and 30 electrocautery). Lesions excised were carcinoma in 30(48%), dysplasia in 31(50%) and benign in 1 (2%). There was no difference in the location of lesion, size of lesion, defect size, type of closure, resection time, and blood loss between Laser and EC arms. Patients who had Laser had less pain compared to EC (mean pain score on POD 7 L = 2.84 vs EC = 3.83, $P = 0.11$). better UW QOL scores and PSS scores, quicker return to

normal diet (median days L = 26.0 vs EC = 28.5, $P = 0.17$) and faster return to work (median days L = 13.0 vs EC = 16.5, $P = 0.14$). However, these results were not statistically significant.

Conclusion: There was a trend for patients treated with laser to have less pain and better quality of life scores but these result were not statistically significant. Based on the actual observed difference, a large multicenter RCT with 90 patients in each arm is required to determine the clinical relevance of our results.

KEYWORDS
laser, Oral cancer, oral premalignant lesions, outcomes, pain, quality of life

1 | INTRODUCTION

The incidence of cancers of the oral cavity and oropharynx is gradually rising in the United States. The American Cancer Society estimates 53 000 new cases or 3% of all new cancers diagnosed in 2019.[1] Because of their location, and development of early symptoms, oral cavity lesions may be found at an early stage by the patient or their dental or primary care provider. Many oral cavity lesions are often detected as premalignant lesions (PML) such as leukoplakia or erythroplakia. These PMLs have the potential for malignant transformation,[2-4] so they are commonly treated with surgical resection.[5]

Depending on the stage, the standard of care for oral cavity cancer includes surgery with or without adjuvant radiation.[6] Surgical resection, the extent of which will depend on the size and location of the lesion, in the oral cavity can often cause significant post-operative sequela.[7] This includes postoperative pain that is a commonly expected consequence of surgery in the head and neck region.[8] It is therefore important to employ techniques that may lead to less morbidity whenever possible. Different surgical cutting devices that may be used during these surgeries include a traditional scalpel, electrocautery, or a carbon dioxide laser. Though each of these techniques may be effective at removing early stage lesions, it has been claimed that the use of the carbon dioxide laser may cause less tissue damage resulting in a smaller coagulation and injury zone leading to more precise margin assessment.[9-11] Less thermal injury should also result in less morbidity, related to post-operative pain and inflammation and quicker return to normal function.[9,10]

The development of the flexible fiber CO_2 laser has allowed the CO_2 laser to be delivered with fine precision using handheld instruments in the oral cavity, oropharynx, larynx, nasal cavity, and middle ear. Indeed, these techniques have been previously studied in the excision of benign and early stage tumors of the oral cavity.[12,13] To date, however, there has been no study which has directly compared its use in the resection of lesions of the oral cavity to traditional electrocautery in terms of postoperative pain and quality of life. Therefore, the purpose of our study was to compare the use of flexible fiber CO_2 laser (OmniGuide) to electrocautery for surgical resection of early-stage and precancerous lesions of the oral cavity, not requiring neck dissection, for postoperative patient reported outcomes. The primary endpoint of our study was pain level at postoperative day (POD) 7. A variety of secondary endpoints, including quality of life and performance, return to work, resection time and blood loss were also included in our analysis.

2 | METHODS

2.1 | Trial design

This was a single center patient-blinded randomized controlled trial comparing postoperative pain and quality of life in patients having surgery for benign lesions, premalignant lesions, or early stage cancers of the (T1) oral cavity treated by CO_2 laser fiber resection vs electrocautery resection. The trial was approved by the Institutional Review Board at Memorial Sloan Kettering Cancer Center (MSKCC) (IRB number 11-034) and was registered with Clinical trials.gov NCT01355926 (https://clinicaltrials.gov/ct2/show/NCT01355926?term=omniguide&cond=Oral+Cancer&cntry=US&state=US%3ANY&city=New+York&draw=2&rank=1).

Patients were recruited from the Head and Neck Service outpatient clinics at MSKCC. Recruitment and treatment protocols occurred between May 2011 and March 2019. All patients signed IRB-approved informed consent forms. Patients were included in the trial based on the following criteria:

1. Biopsy proven diagnosis or clinical diagnosis of premalignant oral cavity lesions (leukoplakia, erythroplakia, lichen planus, dysplasia).
2. Biopsy proven diagnosis of small superficial oral cavity SCC (stage T1N0) requiring resection without the need for neck dissection.
3. Any benign oral cavity lesion. Pre-surgical biopsy not required if lesion was suspected to be benign.
4. All pathology was reviewed at MSK to confirm diagnosis.
5. The lesion plus the resection margin did not exceed 4.0 cm circumferentially. Surgical treatment was by resection without flap reconstruction and without neck dissection.
6. All patients age 18 years of age and older.
7. Karnofsky performance score over 60.
8. Patients on anticoagulants (aspirin or Coumadin) were asked to stop medications 7 days prior to surgery. In the case of Coumadin,

patients were switched to lovenox 7 days prior to surgery and this was stopped the day before surgery. Following surgery aspirin or Coumadin were recommenced 48 hours postoperatively.

The following were exclusion criteria in our patient cohorts: (a) Patients with previous head and neck radiation. (b) Pregnant or lactating female patients. (c) Patients with oral cavity squamous cell cancer requiring neck dissection.

2.2 | Randomization

Randomization was carried out using MSKCC's clinical research database (CRDB). Patients were blinded to the treatment modality used. Randomization was accomplished by the method of random permuted block.

2.3 | Intervention

During surgery, the oral cavity lesion was marked out. A 1 cm margin was then marked for suspected and biopsy proven SCC. A 5 to 10 mm margin was marked out for premalignant oral lesions. The lesion was then excised using either electrocautery or the CO_2 flexible fiber. Specifically:

1. In the electrocautery excised group, the cut and coagulation modes used were each at 25 W power setting. First, cut mode was used to mark out the lesion. Subsequently, coagulation mode was used for excision. Bipolar cautery was used at 25 W for hemostasis.
2. In the CO_2 excised group, the flexible fiber carbon dioxide laser system designed by Omniguide was used. The fiber consists of multiple layers of highly reflective mirrors, which efficiently and safely transmit laser energy through the length of the fiber (see Figure S1). The resection was performed at 15 W, at a distance of 1 cm from the tissue. Here too, if required, the bipolar electrocautery was used to achieve hemostasis.

Frozen section margins were obtained at the discretion of the surgeon as per standard practice using a scalpel for both groups. The size of the resulting oral cavity defect from resection was then measured using calipers to the nearest mm. Representative photographs were taken. The oral cavity defect was either closed primarily, with alloderm graft or left open to heal by secondary intention.

There were 9 surgeons in the trial of whom 3 were frequent laser users. All surgeons were blinded to the details of the primary and secondary outcome measures.

2.4 | Primary outcome

The primary outcome of the study was postoperative pain measured using a numerical pain rating scale. The scale ranges from 0 to 10, with 0 indicating no pain, 1 to 3 indicating mild pain, 4 to 6 indicating moderate pain, and 7 to 10 indicating severe pain. A baseline pain level was assessed in the pre-operative setting. Subsequent ratings were obtained for each patient in the post-operative setting on post-operative day (POD) 1, 3, 7, 14, 21, and 28. The particular focus for this study was pain level on POD 7 because our previous experience suggested this was the period at which pain severity was maximum. The study was therefore powered to detect a group difference on the measure of post-operative pain using the numerical rating scale at 7 days post-surgery. We expected the SD (SD) of pain ratings to be between 2.0 to 2.5 in both groups. Our power analysis additionally assumed a sample size of 30 patients in each arm and a Type I error rate (ie, the probability of observing a group difference when in truth there is none) of 0.05. Under these assumptions, we had power of 0.90 to detect a difference of 1.67 to 2.09 points between the group means on the numerical rating scale using a two-sided independent samples *t*-test. Other studies using the pain scale 0 to 10 have used a difference of 1 point as a clinically important difference.[14,15] Therefore a difference of 1.67 to 2.09 in our study was thought to be clinically significant.

2.5 | Secondary outcomes

Secondary outcome measures that were included in this study were a number of intra-operative parameters, quality of life as well as cost-effectiveness analysis.

2.5.1 | Quality of life

Quality of life, specifically the impact of surgery on speech and swallowing, was assessed using the University of Washington Quality of Life questionnaire specific for head and neck version 4 (UW-QOL version4) and the Performance Status Scale for head and neck cancer (PSS-HN). This was done pre-operatively and on post-operative day (POD) 7, 14, and 28. The UW-QOL questionnaire is a validated QOL measure, which has been previously used for functional assessment of speech, swallowing, and pain in head and neck cancer patients. It consists of a 16-item questionnaire that covers quality of life in 12 domains - pain, appearance, activity, recreation, swallowing, chewing, speech, shoulder function, taste, saliva, mood and anxiety, in addition to 4 global questions. The 12 domain-specific items yield a composite score ranging from 0 to 100. The internal consistency reliability (Cronbach's alpha) of the composite score was 0.86 in the validation study of version 4 of the instrument.[16] It has been extensively prospectively validated and is widely used due to its simplicity, lack of copyright restrictions, simple scoring, and availability of prospectively validated translations in several foreign languages.[17] The PSS-HN was designed to evaluate performance in areas of functioning most likely affected by head and neck cancer and its treatment, specifically eating, speaking and eating in public. It is a clinician rated

TABLE 1 Summary of clinical and tumor characteristics

Variables	Overall N = 62	EC N = 30	Laser N = 32	*P*-value
Sex				.79
Female	33 (53%)	17 (57%)	16 (50%)	
Male	29 (47%)	13 (43%)	16 (50%)	
Race				.032
Asian	2 (3.2%)	1 (3.3%)	1 (3.1%)	
Black	3 (4.8%)	3 (10%)	0 (0%)	
Unknown	6 (9.7%)	5 (17%)	1 (3.1%)	
Caucasian	51 (82%)	21 (70%)	30 (94%)	
Age(mean, SD±)	61 (12)	61 (13)	61 (12)	.98
Location of lesion				.31
Anterior floor of mouth	8 (13%)	4 (13%)	4 (12%)	
Buccal	1 (1.6%)	1 (3.3%)	0 (0%)	
Lateral floor of mouth	5 (8.1%)	4 (13%)	1 (3.1%)	
Lateral tongue	48 (77%)	21 (70%)	27 (84%)	
Pathology				.35
Benign	1 (2%)	0 (0%)	1 (3%)	
Carcinoma in situ	16 (26%)	10 (33%)	6 (19%)	
Dysplasia	15 (24%)	8 (27%)	7 (22%)	
Invasive carcinoma	30 (48%)	12 (40%)	18 (56%)	
Size of lesion[a]	1.20 (0.74, 2.30)	1.20 (0.70, 1.90)	1.20 (0.78, 2.30)	.59
Size of specimen[a]	3.00 (2.50, 3.48)	3.00 (2.50, 3.38)	3.00 (2.50, 3.50)	.79
Type of closure				.52
Alloderm graft	15 (24%)	8 (27%)	7 (22.1%)	
Secondary intention	2 (3%)	1 (3.3%)	1 (3.1%)	
Primary closure	45 (73%)	21 (70.3%)	24 (75%)	

[a]Greatest dimension in cm; Median, IQR.

instrument consisting of three subscales: Normalcy of diet, Understandability of Speech, and Eating in Public. Each is rated from 0 to 100, with higher scores indicating better performance.[18,19]

2.5.2 | Lesion resection time

Prior to excision, the size of the lesion was measured (important for normalizing the time for lesion resection to allow for comparison between lesions). Time of resection was measured by the operating room staff; time began at the time at first incision and ended upon achievement of hemostasis.

2.5.3 | Estimated blood loss

Blood loss was measured by weighing sponges before and immediately after use, and then adding that weight to the volume of blood in the suction apparatus.

2.5.4 | Time to normal diet

Dietary patterns were followed during phone interviews or in the clinic on postoperative days 1, 3, 7, 14, 21 and 28. The assessments on days 1, 3, 7 and 21 were generally conducted by telephone consultation with the allowed deviance of ±1 day. The assessments on postoperative days 14 and 28 (±3 days) were conducted during outpatient visits or by telephone. Diets were categorized as either liquid, pureed, soft diet or normal diet.

2.5.5 | Time to complete healing of wound

Patients were examined at POD 14 and 28 (±3 days) in clinic by the operating surgeon to determine the time for complete healing and mucosalization. Patients whose surgical site had completely healed and mucosalized at the POD 14 visit, and in the opinion of the treating investigator the patient does not need to return to clinic, did not require a POD 28 clinic visit.

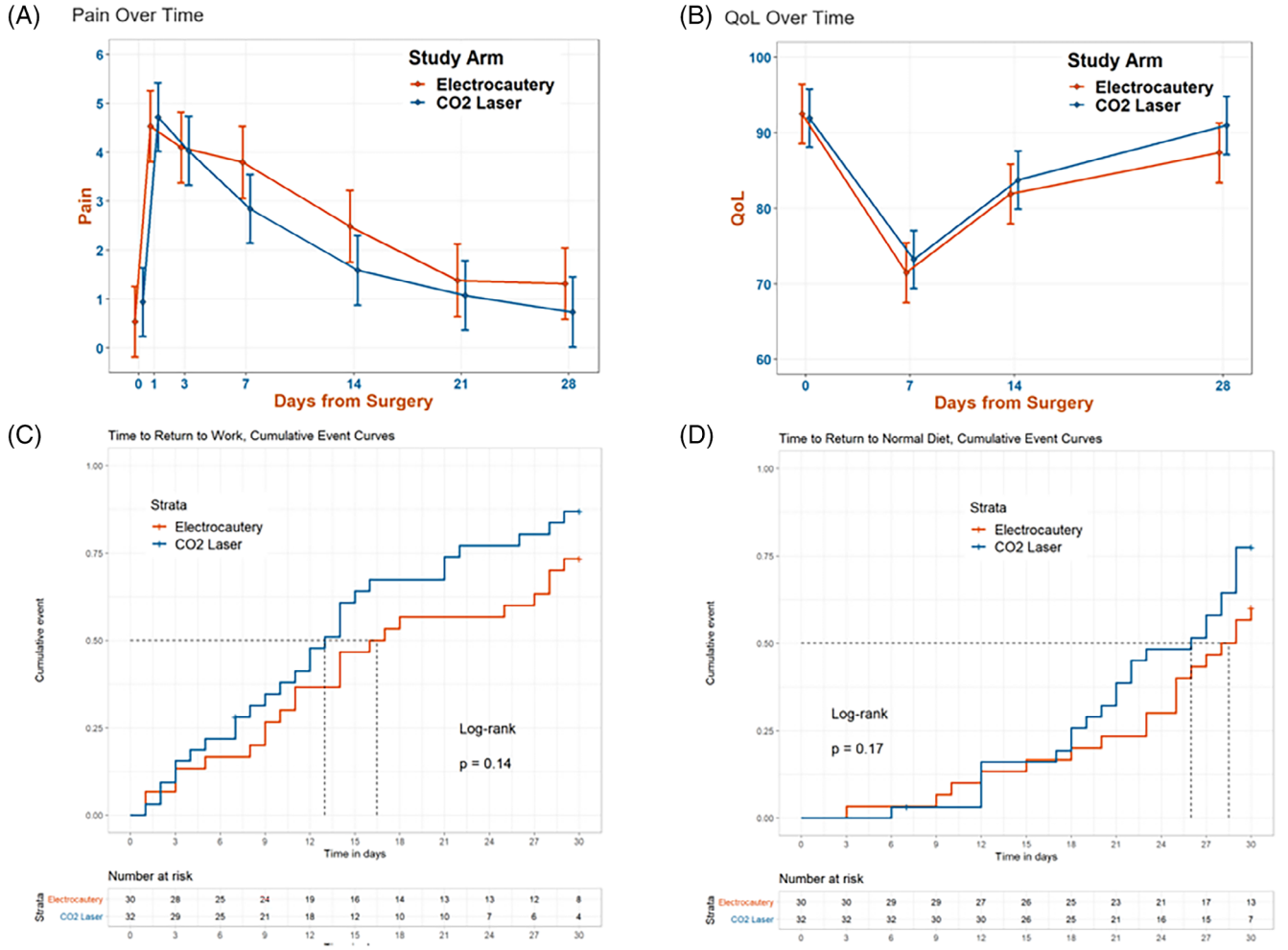

FIGURE 1 Pain scores level at the various postoperative days for laser and electrocautery arms (A). University of Washington quality of life scores at the various postoperative days for laser and electrocautery arms (B). Time to return to normal diet for laser and electrocautery arms (C). Time to return to work for laser and electrocautery arms (D)

2.5.6 | Time to return to work

This was assessed on each telephone call or outpatient visit.

2.6 | Statistical analysis

We calculated the mean and 95% confidence interval (CI) for continuous endpoints by study arm at each assessment time, and we used independent samples t-tests to compare study arms. Estimated blood loss and lesion resection time were both right-skewed, so we summarized these endpoints using medians and interquartile ranges (IQRs), and tested for group differences using Wilcoxon rank sums test. We summarized categorical variables using frequencies and percentages, and we tested for group differences using Fisher's exact tests. We treated time to return to normal diet and time to return to work as time-to-event analyses. We used the Kaplan-Meier method to estimate the cumulative event distributions for those endpoints by study arm and used log-rank tests to compare study arms.

3 | RESULTS

3.1 | Patient and tumor characteristics

Patient and tumor characteristics are shown in Table 1. Overall, 33 (53%) patients were female and 51 (82%) were Caucasian. The mean age was 61 years (SD 12 years). The majority of the oral cavity lesions were located on the lateral border of the tongue (48.77%). Thirty-one (50%) of the lesions were PML, 30 (48%) were T1 cancers and 1 (2%) was benign. The median size of resected lesions was 1.2 cm (range 0.74-2.3) and the median size of the resulting defect was 3.0 cm (range 2.5-3.5). The majority of the lesions were closed primarily (45, 73%) followed by alloderm graft (n = 15, 24%) with only 2 lesions left to heal by secondary intention. Both L and EC groups had comparable numbers of patients with defects closed primarily,

TABLE 2 Summary of pain by time and arm

Time	Arm	N	Mean (95% CI)
Pre-Op	EC	30	0.53 (0.14-0.92)
	Laser	32	0.94 (0.32-1.55)
	(all)	62	0.74 (0.38-1.1)
		Sig.Tests:	*P* = .27
POD 1	EC	30	4.53 (3.55-5.52)
	Laser	32	4.72 (3.96-5.48)
	(all)	62	4.63 (4.03-5.23)
		Sig.Tests:	*P* = .76
POD 3	EC	30	4.1 (3.23-4.97)
	Laser	32	4.03 (3.17-4.89)
	(all)	62	4.06 (3.47-4.66)
		Sig.Tests:	*P* = .91
POD 7	EC	29	3.83 (2.87-4.78)
	Laser	32	2.84 (2.05-3.64)
	(all)	61	3.31 (2.7-3.92)
		Sig.Tests:	*p* = .11
POD 14	EC	29	2.52 (1.57-3.47)
	Laser	31	1.52 (0.95-2.08)
	(all)	60	2 (1.46-2.54)
		Sig.Tests:	*P* = .065+
POD 21	EC	28	1.32 (0.72-1.92)
	Laser	31	1 (0.4-1.6)
	(all)	59	1.15 (0.74-1.57)
		Sig.Tests:	*P* = .44
POD 28	EC	29	1.34 (0.62-2.07)
	Laser	30	0.6 (0.08-1.12)
	(all)	59	0.97 (0.53-1.41)
		Sig.Tests:	*P* = .091+

with alloderm or with secondary intention. Both groups were also comparable for all other variables except for race ($P = .032$).

3.2 | Surgeon characteristics

There were 9 surgeons in the trial of whom 3 carried out 71% of the cases (Table S1). Of the 9 surgeons 3 were frequent users of the laser and therefore had more laser experience. These were surgeons 1, 3, and 6. The other 6 surgeons were EC users. Of the 32 laser cases done, 20 were carried out by the EC users and 12 by the laser users. This indicates the trial may have had a degree of negative bias against the laser arm of the study.

3.3 | Primary endpoint postoperative pain at day 7

The primary endpoint for this study was the pain level in each group on POD 7. Figure 1A and Table 2 summarizes the data for pain level at the various postoperative days on which study participants were surveyed. At POD 7, 14, 21, and 28 the mean pain score in the laser group was less than the electrocautery group. At the primary outcome time point of interest POD 7, the mean pain score for the laser group was 2.84 compared to 3.83 in the electrocautery group. However, this was not statistically significant ($P = .11$). From Figure 1A and Table 2 we also observe that the laser group appears to recover quicker as the pain scores dip down towards baseline earlier in the laser group beginning at POD 7 through to POD 28. When we assess the percentage of patients using analgesia following surgery there was no difference between the EC and L groups. If we categorize by type of analgesia used (opiod and non-opiods) there was also no difference observed (Table S2).

TABLE 3 Summary of quality of life by time and arm

UW-QOL	Arm	N	Mean (95% CI)
Pre-Op	EC	30	92.51 (89.65-95.37)
	Laser	32	91.94 (88.99-94.89)
	(all)	62	92.22 (90.22-94.22)
		Sig.Tests:	*P* = .78
POD 7	EC	30	71.48 (67.42-75.53)
	Laser	32	73.23 (68.57-77.9)
	(all)	62	72.38 (69.36-75.41)
		Sig.Tests:	*P* = .57
POD 14	EC	30	81.91 (77.17-86.65)
	Laser	31	83.98 (79.79-88.16)
	(all)	61	82.96 (79.89-86.04)
		Sig.Tests:	*P* = .51
POD 28	EC	30	87.37 (82.92-91.82)
	Laser	31	91.22 (87.02-95.43)
	(all)	61	89.33 (86.32-92.34)
		Sig.Tests:	*P* = .2

3.4 | Secondary endpoints

3.4.1 | University of Washington Quality of Life (UW-QOL)

Figure 1B and Table 3 summarizes the UW-QOL scores at the various postoperative days. Preoperatively the groups were not significantly different in QoL ($P = .78$). QoL was lowest at POD 7, and in both groups returned toward baseline quality of life by POD 28. For the electrocautery group, preop QoL score was 92.51 and POD 28 QoL score was 87.37. For the laser group, preop QoL score was 91.94 and POD 28 QoL score was 91.22. There was no statistically significant differences between the groups. However, there was a trend for the laser group to have better QoL scores at all time points in the postoperative period.

3.4.2 | Performance Status Scale for head and neck cancer (PSS-HN)

Table S3, Figure S2 summarizes the PSS-HN scores for diet, speech, public eating and composite. The mean (95% CI) scores are shown.

Overall, scores for diet, speech and public eating were lowest at POD 7 and gradually returned to baseline scores by POD 28 in both groups. There was no statistically significant differences between the groups. However, there was a trend for the laser group to have better PSS-HN scores at all time points in the postoperative period.

3.4.3 | Blood loss, lesion resection time, healing time

Table S4 summarizes the blood loss, resection times and healing time for both groups. There was no difference in the volume of blood loss between groups (Median 6.6 mL for EC vs 8.4 mL for Laser, $P = 0.64$). The resection times for both groups were also similar (Median 14.5 minutes for both groups, $P = .51$). Overall, 28 (46%) patients had healed by POD 14, 24 (39%) by POD 28 and 9 (15%) healing after POD 28. There was no difference in healing times between the 2 groups.

3.4.4 | Time to return to normal diet and return to work

Some patients had not returned to work (n = 13) or resumed a normal diet (n = 20) by the time the study ended. As such, a survival analysis method is the preferred way to examining these time dependent endpoints. From Figure 1C we can see that patients in the laser group returned to normal diet quicker than the EC group ($P = .17$). In addition, patients in the laser group also returned to work faster than the EC group ($P = .14$) (Figure 1D). These results were not statistically significant however.

4 | DISCUSSION

The objective of our study was to carry out a single-center randomized controlled trial, comparing postoperative pain and quality of life in patients having surgical resection of early stage or premalignant oral cavity lesions (PMLs) with either electrocautery or with CO_2 laser. Our study showed there was a trend for patients treated with laser to have less pain, better quality of life scores, and faster return to normal diet and work compared to patients treated with electrocautery. However, these differences were not statistically significant.

The use of the CO_2 laser for the resection of oral cavity cancer using transoral laser microsurgery (TLM) is now accepted as a technique which gives comparable oncological outcomes to non-TLM techniques but arguably with improved functional outcomes. The technique utilizes that described by Steiner.[20] Under the operating microscope radial transtumoral incisions are made into the tumor to assess depth and the tumor is then removed in blockwise fashion. The technique allows depth of tumor to be assessed with the microscope and then confirmed with frozen section. The technique results in a more personalized approach to tumor resection limiting the amount of normal tissue excised thus preserving function. Using this technique Sinha et al[21] reported results in 95 patients with OSCC treated with TLM with neck dissection, 71 were T1T2 and 24 T3T4a cancers. The 5 year local control rate was 78% for the whole cohort, 78% for T3 tumors and 69% for T4 tumors. The 5 year DSS for the whole cohort was 76% and OS 65%. These results were comparable to and superior to some studies utilizing non-TLM surgery. Similar results have been reported by Eckel et al[22] and also by Jerjes et al.[23] However, there is very little in the literature reporting on the postoperative pain and quality of life in patients treated with laser surgery and no randomized trials comparing laser to standard techniques. In our study we focused primarily on patients who did not need neck dissections and therefore the cohort comprised patients with PMLs or very early T1 cancers.

PMLs are estimated to transform into squamous cell carcinoma at a rate of 1% per year.[3] The standard of care for PMLs and early stage oral cavity cancer has been long established as surgical resection.[24] Though the technique of this surgery has evolved over the years, surgeons today rely on either electrocautery, standard scalpels, or carbon dioxide lasers. Our focus was the postoperative outcomes for patients randomized to either carbon dioxide laser or electrocautery resection. The use of the flexible carbon dioxide laser in surgical resection of head and neck tumors has been studied for many years.[25,26] More specifically, decades of research have shown that the laser is an effective means of resection for premalignant oral cavity lesions.[24,27] A recent systematic review summarized the literature behind the use of carbon dioxide laser in the resection of PMLs. This study concluded that there were benefits in terms of post-operative complications favoring the use of laser in these surgeries.[28] Devaiah et al theorized that technical challenges have prevented widespread use of these lasers until the development of a flexible fiber mechanism.[29]

In this study we used the OmniGuide flexible fiber carbon dioxide laser. This is a flexible fiber laser which comprises of multiple layers of highly reflective mirrors, which efficiently and safely transmit laser energy through the length of the fiber. The OmniGuide laser has been previously studied for use in resection of tumors in other sites of the head and neck such as the oropharynx[30] and the larynx.[29,31] Of note, Karaman et al specifically demonstrated benefit of the Omniguide laser when compared to electrocautery for resections in the oropharynx. They noted lower levels of postoperative pain in their laser cohort when compared to the electrocautery cohort.[30] In addition to head and neck sites, these lasers have recently been studied in the neurosurgical environment, where they were shown to be a valuable tool in the resection of vestibular schwannomas.[32,33] This research demonstrates various benefits to these instruments in anatomical locations where preserving function is vitally important. Given that the oral cavity is necessary for speech and swallowing, exploring function preserving techniques, like the use of the carbon dioxide laser, in this region should be a focus of ongoing research.

In our single-center randomized controlled trial, we found no statistically significant difference in the primary outcome measure of postop pain at day 7. Although the results were not statistically significant, it is important to note that our observed difference in pain

ratings between the two arms (SMD = 0.42) was substantially smaller than the SMD of 0.835 or larger that our study was powered to detect. There was a numeric difference between the pain score of the two groups at the POD 7 time point (EC 3.83 vs Laser 2.84). In addition the differences at POD 14 and POD 28 were marginally statistically significant ($P < .1$). This suggests a difference between the two groups does exist. Other studies using the pain scale 0 to 10 have used a difference of 1 point as a clinically important difference.[14,15] In our study we did have a 1 point difference at POD 14 and almost at POD 7. Therefore, one may argue that our results are clinically relevant even though not statistically significant. In our study, the difference between the arms in POD7 pain means was 0.984, and the pooled SD at POD7 was 2.35. This resulted in a standardized mean difference effect size (aka, Cohen's *d*) of 0.42 (95% CI: −0.10, 0.94) at POD7. For a future study to have 80% power to detect an effect size of 0.42 between the arms, 90 patients will need to be enrolled to each of the two arms. This calculation assumes a two-sided independent samples *t*-test and type I error rate (alpha) of 0.05. To carry out this study would entail a larger multicenter trial.

In our study we also observed a trend towards better quality of life, faster return to normal diet and return to work in the laser arm. Both treatment groups showed returns toward baseline quality of life, with a numeric difference between the groups on POD 28 (87.37 for EC vs 91.22 for laser) but this was not statistically significant. Given the possibility of type II error for postoperative pain, it may also be the case that there may also be a difference in QoL for these two groups as well. If indeed there is a difference in QoL for these groups, it may be secondary to the difference in pain levels between the two surgical techniques.

A similar study published by Chee and Sasaki also compared the use of cold steel and carbon dioxide laser for surgical resection of leukoplakia. They found no significant difference in their primary endpoints of resection time and blood loss.[34] These results were confirmed in our study. They reported no difference in postoperative pain between the groups. However, many of their patients required neck dissection which was thought by the authors to confound the pain results. In contrast, our study is unique in its design as we specifically did not recruit any patients who required a neck dissection thus eliminating the effect of this type of surgery as a confounder for pain.

In addition to the impact on pain and quality of life, the choice of using laser resection in preference to traditional electrocautery must also take into account surgeon preference, availability, and ease of use of laser and of course the economic cost of using laser. At present the cost of the omniguide laser fiber is 100× more expensive than the cost of electrocautery. In some health care systems this may be unjustified and the use of laser in these scenarios would be at the patient request with the agreement to pay the differential cost of care. Alternatively other laser fibers could be used at reduced cost. The fiberlase CO_2 laser fiber manufactured by Lumenis and the Flexiva laser fiber manufactured by Boston Scientific are recent examples of laser fibers introduced at a reduced cost.

4.1 | Limitations

Many patients with early stage oral cavity cancer undergo elective neck dissection as part of their treatment plan. This limited the number of patients with early stage oral cancer who were eligible for our study. As a result, this made recruitment of appropriate patients to our study extremely difficult. Our power analysis based upon the actual difference between the 2 groups suggests 90 patients in each group would be required to be significant. Therefore, a multicenter randomized controlled trial would be required for this larger cohort of patients. We anticipate a multi-institutional trial with 10 centers (18 patients per institution) would be able to recruit this number of patients over a 2 year period. Another limitation in our study was the choice of POD7 as the optimum time to assess postoperative pain. It is possible that the optimal assessment of pain may be at a different time point such as POD 14 or possibly a time point in between such as POD 10. In addition, it is possible that a 1 point difference on the pain score may be clinically relevant and a more appropriate difference to use for sample size calculations. Lastly, there may be heterogeneity in patients pain tolerance. By randomizing patients, we would hope to reduce this effect but it is possible this may not be fully controlled for.

4.2 | Conclusion

In conclusion, this study showed there was a trend for patients treated with laser to have less pain, better quality of life scores, and faster return to normal diet and work compared to patients treated with electrocautery. However, these differences were not statistically significant. Based upon a power analysis of the actual difference in pain POD7 that we observed, a larger multicenter randomized controlled trial with 90 patients in each arm is required to improve the statistical significance of our results. Such a trial would have important clinical significance. Less pain and morbidity results in improved patient function and satisfaction. It also has an impact on the use of opioid medications. Many patients having surgery on the oral cavity require opioid medications for pain control in the postoperative setting. Pang et al recently published study that showed that postoperative use of opioid medications can lead to chronic opioid use.[35] If there is a possibility to prevent chronic opioid use by decreasing the acute tissue injury and pain using the carbon dioxide fiber laser, then these results should be explored with further research into the expansion of carbon dioxide laser in these surgeries.

CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

TRIAL REGISTRATION

Clinical trials.gov NCT01355926 (https://clinicaltrials.gov/ct2/show/NCT01355926?term=omniguide&cond=Oral+Cancer&cntry=US&state=US%3ANY&city=New+York&draw=2&rank=1).

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

How to cite this article: Rosenthal M, Baser RE, Migliacci J, et al. Flexible fiber-based CO_2 laser vs monopolar cautery for resection of oral cavity lesions: A single center randomized controlled trial assessing pain and quality of life following surgery. *Laryngoscope Investigative Otolaryngology*. 2021;6:690–698. https://doi.org/10.1002/lio2.572