

## Original Article

# Low-temperature plasma radiofrequency ablation is effectively treats early glottic carcinoma

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**Abstract:** Objective: To evaluate the treatment efficacy of low-temperature plasma radiofrequency ablation (LTP-RFA) in patients with early glottic carcinoma (EGC). Methods: A total of 80 EGC patients were retrospectively selected and divided into a control group (standard laryngofissure) and a research group (LTP-RFA) based on their treatment methods. Surgery-related indicators, visual analogue scale (VAS) and mucosal recovery scores, efficacy, serum indices, voice acoustics (amplitude perturbation, fundamental frequency perturbation, harmonic-to-noise ratio), European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTCQLO-C30) scores, complications, and postoperative recurrence were compared between the two groups. Results: Compared to the control group, patients in the LTP-RFA group demonstrated markedly shorter surgery time, less intraoperative blood loss, and reduced length of hospital stay. In addition, postoperative VAS score, mucosal recovery score, and the total complication rate were all lower in the research group, with a higher overall effective rate. The research group also exhibited greater reductions in post-treatment serum biomarker levels (e.g., matrix metalloproteinase-9 (MMP-9), nitric oxide (NO), or vascular endothelial growth factor (VEGF)), better improvements in acoustic parameters (e.g., amplitude perturbation, fundamental frequency perturbation, and harmonic-to-noise ratio) than the control group, along with higher total EORTCQLO-C30 scores. The recurrence rate was equivalent in the two groups. Conclusion: LTP-RFA is an effective treatment for EGC, offering advantages in improving therapeutic efficacy, voice acoustics, as well as reducing postoperative complications.

**Keywords:** Low-temperature plasma radiofrequency ablation, early glottic carcinoma, therapeutic outcomes, voice acoustics, complications

## Introduction

Classified as Tis-T2 lesions, early glottic carcinoma (EGC) is characterized by the absence of cervical lymph node invasion and distant metastasis [1]. As a subtype of head and neck malignancies, EGC accounts for approximately 1% of the global cancer burden with a steadily increasing incidence [2, 3]. In 2020 alone, more than 180,000 new cases of EGC were reported globally, with nearly 100,000 deaths. The glottis is the most commonly affected site, accounting for about 70% of cases, and from a pathologic perspective, squamous cell carcinoma is the predominant histologic type [4]. EGC generally has a favorable prognosis, evidenced by a 5-year overall survival rate (OS) of up to

95% [5]. This may be related to the high specificity of early clinical manifestations, including vocal acoustic abnormalities (e.g., hoarseness, voice changes, difficulty in phonation), as well as possible complications like respiratory distress and massive bleeding [6, 7].

A conventional laryngofissure procedure is often employed for EGC cases. This technique provides excellent exposure of the laryngeal cavity, ensuring an unobstructed surgical field. It helps accurately locate and remove lesions while also reducing improper irritation and damage to the laryngeal mucosa [8]. However, this treatment method is not without drawbacks. One major concern is significant surgical trauma and a frequent need for tracheotomy. These

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factors increase the risk of postoperative complications such as voice disorders, swallowing difficulties, cervical scarring, and incision-related infections [9].

Low-temperature plasma radiofrequency ablation (LTP-RFA) may compensate for the disadvantages of traditional laryngofissure, featuring minimally invasive, high safety, and the ability to preserve laryngeal functions as much as possible [10]. This may be attributed to the low-temperature characteristic of this therapy (40-70°C), which reduces thermal injury and avoids tissue burns [11]. LTP-RFA has been successfully applied in the treatment of various conditions, including primary thyroid-like low-grade nasopharyngeal adenocarcinoma, lingual cysts, and Barrett's esophagus-related developmental disorders, demonstrating certain clinical advantages and feasibility [12-14]. Moreover, its application in laryngeal leukoplakia has been shown to promote postoperative recovery of vocal cord morphology and function [15]. In the report by Wang et al. [16], LTP-RFA was clinically advantageous over CO<sub>2</sub> laser surgery in EGC patients, significantly shortening surgical duration and facilitating postoperative mucosal recovery, though with a relatively higher intraoperative blood loss.

However, there are relatively few clinical studies on this therapy for EGC. Therefore, this study aimed to address this gap by systematically evaluating the clinical efficacy and safety of LTP-RFA, thereby providing additional references for decision-making in EGC management.

### Materials and methods

#### *Patient selection*

Eighty EGC cases were retrospectively selected (January 2020-January 2025), following approval from the Ethics Committee of Tongren Hospital, Shanghai Jiao Tong University School of Medicine. Among these patients, 35 patients underwent conventional laryngofissure surgery and were assigned into the control group, while 45 received LTP-RFA and comprised the research group.

Inclusion criteria: (1) pathologically confirmed early glottic squamous cell carcinoma [4]; (2) presence of relevant clinical manifestations

(e.g., hoarseness, sore throat); (3) no prior anti-tumor treatment; (4) physically feasible without anesthesia or surgical contraindications; (5) absence of regional lymph node metastasis by preoperative cervical ultrasound/computed tomography (CT); (6) normal cognitive and communicative abilities; (7) medical record completeness; (8) completion of a 12-month follow-up.

Exclusion criteria: (1) history of neck surgery; (2) pregnancy or lactation; (3) severe dysfunction of major organ (e.g., heart, lungs, liver, kidneys) or serious systemic diseases; (4) coagulopathies or autoimmune deficiencies; (5) severe acute/chronic infections; (6) other malignant diagnoses; (7) treatment contraindications.

#### *Intervention methods*

All surgeries were performed by the same team of doctors. Routine preoperative evaluations, including laryngoscopy, cervical lymph node color Doppler ultrasound, and enhanced CT scans were performed to assess tumor invasion extent.

Patients in the control group underwent traditional laryngofissure. Following general anesthesia with the patient lying supine, routine skin preparation was carried out. A longitudinal midline incision of approximately 2.5 cm was made on the anterior neck midline. The skin, subcutaneous tissue, and strap muscles were dissected layer by layer to fully expose the trachea while preserving the thyroid isthmus. A tracheostomy was subsequently performed by incising the second or third tracheal ring, and then an endotracheal tube was inserted, secured, and connected to a ventilator for assisted breathing. A vertical midline neck incision was made to expose the thyroid cartilage, and a portion of its lamina was removed. Next, the outer membrane was dissected from the upper notch of the thyroid cartilage, and an arc-shaped incision was made into the laryngeal cavity. The extent of tumor invasion was examined, and the lesion was excised with a surgical margin of 3-5 mm. After hemostasis and irrigation of the surgical cavity, the perichondrium of thyroid cartilage was sutured to reconstruct the laryngeal cavity. The laryngeal cavity was closed, and the anterior cervical muscles, subcutaneous tissue, and skin were sutured layer

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by layer. Pressure bandaging was applied, and a cuffed endotracheal tube was replaced. Postoperatively, nasogastric feeding was given.

Patients in the research group were treated with LTP-RFA using a plasma radiofrequency system and an endoscopic laryngoscope. Under general anesthesia, patients were placed supine, and a dental pad was inserted into the mouth for teeth protection. A supporting laryngoscope was introduced trans-orally to expose the glottis and laryngeal cavity. Under the endoscope, the extent of the glottic lesion was examined. Plasma radiofrequency ablation and hemostasis were conducted with the power set to 7 and 3, respectively. Following delineation of lesion boundaries, the tumor was lifted using laryngeal forceps and subsequently abated using a plasma knife, with resection margin of 3-5 mm. The vocal ligaments were protected during the procedure. The excised tissue was sent for intraoperative pathological analysis. Resection was terminated if the resection margin was negative; if positive, additional ablation was performed until complete tumor removal was achieved. For minor intraoperative bleeding, plasma knife tip electrocautery was used for hemostasis, while significant bleeding was managed with bipolar electrocautery. No tracheotomy or wound suturing was required. Routine tracheal intubation or nasogastric feeding was not necessary postoperatively.

Both groups received regular anti-infection treatment for 3 to 5 days post-surgery. Radiotherapy was scheduled at postoperative week 3. Electronic laryngoscopic re-examinations were conducted at 1, 2 and 4 weeks after the surgery. During the first postoperative year, re-examinations were performed monthly. Thereafter, re-examinations were conducted every 3 months to observe the patient's recovery progress.

### *Data collection*

(1) Operation-related metrics. Intraoperative blood loss, surgical duration, and length of hospitalization were recorded for both cohorts.

(2) Postoperative pain and mucosal recovery. Pain assessment employed the Visual Analogue Scale (VAS) [17]; The score (0-10) increases as the pain intensifies. Patients underwent weekly laryngoscopic follow-up examinations over the 4-week postoperative period to assess wound

mucosal healing [18]: time to wound pseudo-membrane shedding  $\leq 7$  days with mucosal smoothing: 1 point; 8-14 days: 2 points; 15-21 days: 3 points; 22-28 days: 4 points; and  $>28$  days: 5 points.

(3) Therapeutic efficacy. Treatment efficacy was evaluated according to established criteria [19]: Marked effectiveness: complete symptomatic resolution (pharyngeal discomfort, hoarseness) with preservation of swallowing and phonatory functions; Effectiveness: Significant symptomatic improvement with largely preserved function; Ineffectiveness: No improvement or symptom deterioration with impaired swallowing and phonatory functions.

(4) Serum biomarkers. A 5-mL fasting venous blood sample was collected from each subject. Following centrifugation, serum levels of matrix metalloproteinase-9 (MMP-9) and vascular endothelial growth factor (VEGF) were measured by enzyme-linked immunosorbent assay (ELISA), while nitric oxide concentration was determined using the nitrate reductase technique.

(5) Voice acoustics. Voice assessments were conducted preoperatively and at 3 months postoperatively. Acoustic analysis was performed using a voice analyzer in an environment with background noise below 45 dB. The patient was instructed to produce the "a" sound while sitting, for a duration of more than 3 seconds. The amplitude perturbation, fundamental frequency perturbation, and harmonic-to-noise ratio (HNR) were analyzed.

(6) Quality of life (QoL). The 30-item European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) [20] was used to assess QoL. This tool measures QoL across five functional scales, three symptom scales, a global health status scale, and six single-item measures. Higher total scores (28-112) indicate better QoL.

(7) Complications. Postoperative complications, including hemoptysis, pharyngeal fistula, surgical site infection, respiratory difficulty, glottic stenosis/adhesion, and wound granulation, were recorded. The incidence of each complication and the overall complication rate were calculated.

(8) Postoperative recurrence. Patients were followed for 12 months by both telephone calls

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**Table 1.** Comparison of patient baseline data between the two groups

Data	Control group (n=35)	Research group (n=45)	$\chi^2/t$	P
Sex			0.438	0.508
Male	25 (71.43)	29 (64.44)		
Female	10 (28.57)	16 (35.56)		
Age (years)	53.60±7.73	51.76±9.30	0.944	0.348
Body mass index (kg/m <sup>2</sup> )	22.46±2.10	23.01±2.26	1.113	0.269
TNM staging			0.911	0.634
Tis	6 (17.14)	5 (11.11)		
T1a	20 (57.14)	25 (55.56)		
T1b	9 (25.71)	15 (33.33)		
Differentiation			0.181	0.670
Well differentiated	30 (85.71)	40 (88.89)		
Poorly differentiated	5 (14.29)	5 (11.11)		
Family history				0.649
No	32 (91.43)	43 (95.56)		
Yes	3 (8.57)	2 (4.44)		

Note: TNM, Tumor, Node, Metastasis.

and outpatient visits. Recurrence rates at 3, 6, and 12 months postoperatively were documented and compared between groups.

Among these measures, surgical-related metrics, postoperative pain/mucosal recovery scores, therapeutic effects, serum indices, voice acoustics, complications, and postoperative recurrence were designated as primary outcomes, while quality of life was a secondary outcome.

### Statistical methods

Statistical analyses were performed using SPSS 20.0 while data visualization was conducted using GraphPad Prism 7.0. Continuous variables were presented as mean ± standard deviation (SD) or median (interquartile range) M [Q1, Q3]. Between-group comparisons were performed using unpaired t-tests, while within-group comparisons of pre- and post-treatment assessments were analyzed using paired t-tests. Group comparisons for categorical data were expressed as n [%] and compared using the  $\chi^2$  tests. A two-sided *P*-value <0.05 was considered significant.

## Results

### Baseline characteristics

As shown in **Table 1**, comparison of patient baseline characteristics revealed no significant

differences in sex, age, body mass index (BMI), TNM staging, differentiation, or family history between the two groups (*P*>0.05), indicating inter-group comparability.

### Operation-related data

Surgery-related data are summarized in **Table 2**. In comparison to controls, the research group demonstrated marked reductions in intraoperative blood loss, operation duration, and hospitalization length (*P*<0.001).

### Postoperative pain and mucosal recovery

Between-group comparisons of postoperative pain and mucosal recovery (**Table 3**) showed markedly reduced VAS scores and superior mucosal recovery in the research group compared to the control group (*P*<0.001).

### Therapeutic outcomes

The overall effectiveness rate was 88.89% in the research cohort and 71.43% in the control cohort, demonstrating superior efficacy in the research group (*P*<0.05) (**Table 4**).

### Serum biomarkers

Serum biomarker levels of both cohorts are summarized in **Figure 1**. At baseline, MMP-9, NO, and VEGF showed no significant intergroup difference (*P*>0.05). Following treatment, a marked suppression was observed in all measured indices for both cohorts (*P*<0.05). Notably, the research group demonstrated markedly lower values across all biomarkers compared to the control group (*P*<0.05).

### Vocal acoustics

The vocal acoustic data of the two groups are shown in **Figure 2**. No significant baseline differences were observed in amplitude perturbation, fundamental frequency perturbation, or the HNR (*P*>0.05). Intervention resulted in a significant decline in both perturbation measures and a rise in the HNR in both cohorts (*P*<0.05). Inter-group comparison confirmed that the research group achieved significantly

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**Table 2.** Comparison of operation-related metrics between the two groups

Indicator	Control group (n=35)	Research group (n=45)	t/Z	P
Intraoperative blood loss (mL)	59.34±15.34	10.11±3.06	21.033	<0.001
Operation duration (min)	49.51±6.15	17.71±5.23	24.983	<0.001
Hospitalization duration (d)	8.00 (7.00, 9.00)	4.00 (3.00, 6.00)	6.370	<0.001

**Table 3.** Comparison of postoperative pain and mucosal healing scores between the two groups

Indicator	Control group (n=35)	Research group (n=45)	Z	P
VAS (points)	4.00 (3.00, 5.00)	3.00 (2.00, 3.00)	4.131	<0.001
Mucosal recovery score (points)	4.00 (3.00, 4.00)	2.00 (1.00, 3.00)	5.008	<0.001

Note: VAS, Visual Analogue Scale.

**Table 4.** Comparison of therapeutic efficacy between the two groups

	Control group (n=35)	Research group (n=45)	$\chi^2$	P
Marked effectiveness	14 (40.00)	23 (51.11)		
Effectiveness	11 (31.43)	17 (37.78)		
Ineffectiveness	10 (28.57)	5 (11.11)		
Overall effectiveness	25 (71.43)	40 (88.89)	3.940	0.047

lower perturbation values and a higher HNR than the control group ( $P<0.05$ ).

### QoL assessment

QoL in both cohorts was assessed using the EORTC QLQ-C30 questionnaire. As presented in **Table 5**, no significant differences were observed in total scores between the two groups at baseline or at 3 months post-treatment ( $P>0.05$ ). By 6 months, both groups exhibited a pronounced increase in scores ( $P<0.05$ ), with the research group achieving significantly superior outcomes relative to controls ( $P<0.05$ ).

### Postoperative complications

Postoperative complications are summarized in **Table 6**, including hemoptysis, pharyngeal fistula, surgical site infection, breathing difficulty, glottic stenosis/adhesion, and wound granulation. The overall complication rate was significantly lower in the research group than in controls (8.89% vs. 28.57%,  $P<0.05$ ) (**Table 6**).

### Recurrence rates

All patients completed a 12-month follow-up. A comparative analysis of recurrence rate

revealed no significant differences between groups at the 3-, 6-, or 12-month postoperative intervals ( $P>0.05$ ) (**Table 7**).

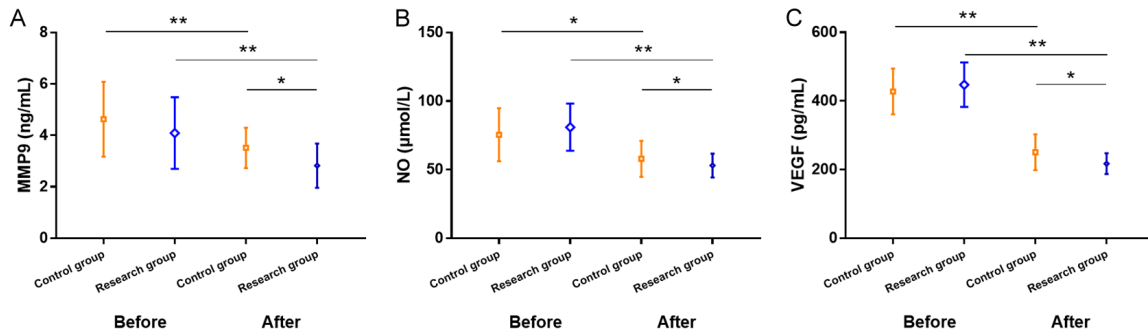
### Discussion

This study compared LTP-RFA with conventional laryngofissure for early glottic cancer (EGC), with a focus on therapeutic efficacy, voice quality, and complications. The results are intended to provide evidence-based guidance for clinicians in selecting optimal surgical interventions for EGC.

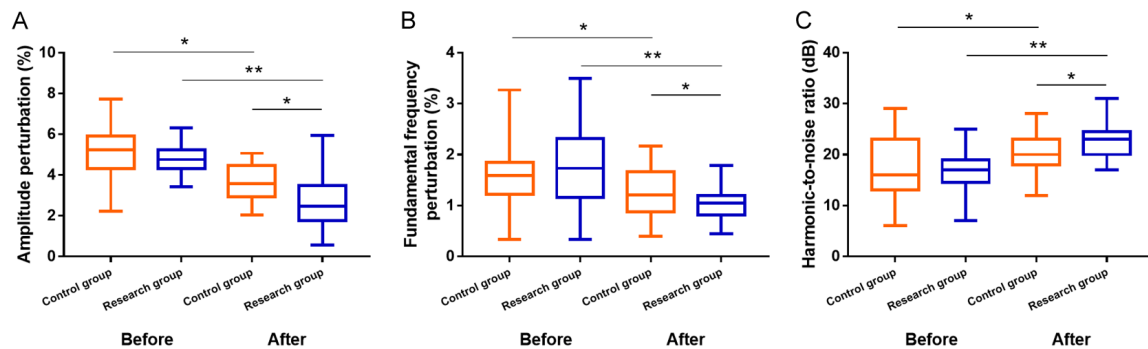
We first observed that LTP-RFA-treated EGC patients exhibited notably less intraoperative blood loss, shorter surgical duration, and reduced hospital stay compared to conventional laryngofissure-managed cases. Additionally, the research group exhibited significantly lower VAS scores and better mucosal healing outcomes. This is because LTP-RFA can achieve multi-angle tissue ablation and simultaneous hemostasis, thereby minimizing intraoperative bleeding, shortening operation time, and promoting postoperative recovery of patients. LTP-RFA, as reported by Zhu et al. [21], is superior to partial laryngofissure in treating EGC, including reduced tissue trauma, less bleeding, fewer postoperative complications, shorter operative and hospitalization durations, and effective vocal function restoration, aligning with our observations. Similarly, Zhang et al. [22] demonstrated that LTP-RFA in treating pediatric pharyngeal tumors exhibited a strong safety profile, minimal invasiveness, and high precision. It can provide a clear surgical field, partially explaining the improved surgical results in



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**Figure 1.** Comparison of serum biomarker levels between the two groups before and after treatment. A. MMP-9 levels. B. NO levels. C. VEGF levels. Note: MMP9, matrix metalloproteinase 9; NO, nitric oxide; VEGF, vascular endothelial growth factor. \*P<0.05; \*\*P<0.01.



**Figure 2.** Comparison of vocal acoustic parameters between the two groups before and after treatment. A. Amplitude perturbation. B. Fundamental frequency perturbation. C. Harmonic-to-noise ratio. Note: \*P<0.05; \*\*P<0.01.

**Table 5.** Comparison of quality of life scores between the two groups

Indicator	Control group (n=35)	Research group (n=45)	t	P
Pre-treatment	63.43±6.06	65.67±7.99	1.378	0.172
3 months post-treatment	71.71±8.70*	73.84±7.35**	1.186	0.239
6 months post-treatment	87.49±7.53***	92.98±7.53***	12.533	<0.001

Note: Compared to pre-treatment, \*P<0.05, \*\*P<0.01, \*\*\*P<0.001.

**Table 6.** Comparison of complication rates between the two groups

Indicator	Control group (n=35)	Research group (n=45)	$\chi^2$	P
Hemoptysis	1 (2.86)	0 (0.00)		
Pharyngeal fistula	2 (5.71)	2 (4.44)		
Surgical site infection	3 (8.57)	1 (2.22)		
Breathing difficulty	2 (5.71)	1 (2.22)		
Glottic stenosis/adhesion	1 (2.86)	0 (0.00)		
Wound granulation	1 (2.86)	0 (0.00)		
Total	10 (28.57)	4 (8.89)	5.283	0.022

LTP-RFA-treated patients. Furthermore, this technique significantly mitigates pain in pa-

tients with recurrent acquired nasolacrimal duct obstruction, supporting the findings in this study [23]. In addition, Shuang et al. [24] demonstrated that radiofrequency ablation was more effective than carbon dioxide (CO<sub>2</sub>) laser in promoting mucosal regeneration and vocal recovery in EGC cases, mirroring our observations.

LTP-RFA significantly enhanced curative efficacy in patients with EGC from 71.43% (traditional laryngofissure) to 88.89%, while more substantially

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**Table 7.** Comparison of the incidence of recurrence between the two groups

Recurrence rate	Control group (n=35)	Research group (n=45)	$\chi^2$	P
3 months postoperatively	0 (0.00)	0 (0.00)	-	-
6 months postoperatively	2 (5.71)	1 (2.22)	0.665	0.415
12 months postoperatively	4 (11.43)	2 (4.44)	1.384	0.239

downregulating serological biomarkers including MMP-9, NO, and VEGF. A previous study indicated that LTP-RFA delivered better therapeutic outcomes compared to traditional surgical procedures for elderly laryngeal cancer patients [25]; the study also showed notable down-regulation in tumor markers (e.g., carbohydrate antigen [CA]125, CA199, and carcinoembryonic antigen [CEA]), as well as suppression of cyclooxygenase-2 (COX-2) and VEGF in laryngeal cancer tissues, complementing our findings. Furthermore, EGC-affected individuals treated with LTP-RFA experienced notable vocal acoustic improvement and QoL enhancement. This may be attributed to the minimally invasive nature of LTP-RFA, which reduces surgical trauma to laryngeal structures and preserves vocal cord integrity, thereby facilitating epithelial regeneration at the surgical site and promoting voice recovery. The favorable surgical efficacy of LTP-RFA, featured a marked reduction in postoperative pain, effective restoration of voice function, and an acceptable clinical safety profile. Collectively, these aspects contributed to the improvements in postoperative QoL.

Finally, LTP-RFA significantly reduced the overall complication rate in EGC patients compared with conventional laryngofissure (28.57% vs. 8.89%), including hemoptysis, pharyngeal fistula, surgical site infection, breathing difficulty, glottic stenosis/adhesion, and wound granulation. However, the recurrence rate during the 12-month follow-up period did not differ substantially between groups. The clinical safety of LTP-RFA may be attributed to rapid lesion ablation, low-temperature coagulation without tissue carbonization, absence of radiation, and precise control of cutting depth, all of which can minimize the impact of thermal injury on normal tissues. Additionally, unlike traditional laryngofissure, LTP-RFA does not involve the neck and tracheal incisions, thus reducing surgery-related trauma, facilitating postoperative recovery, and lowering the risk of complica-

tions. As reported in Yao et al.'s work [26], LTP-RFA has distinct clinical safety profiles when compared to traditional surgeries, causing no sinus hemorrhage or infectious complications, consistent with the results obtained in this research. Jing et al. [27] reported

comparable overall survival (OS) and progression-free survival (PFS) between LTP-RFA and conventional laryngofissure in EGC treatment. However, the former showed higher efficacy in improving acoustic parameters, consistent with our findings.

Previous studies have also proposed new treatment approaches for EGC patients. For instance, Zhu et al. [28] pointed out that endoscopic laser surgery plus nano-silver antibacterial dressings is more effective than endoscopic laser surgery in combination with traditional sterile petrolatum gauze in relieving postoperative dressing pain, promoting wound recovery, shortening hospital stay, and improving the quality of life of EGC patients. Additionally, Ahmadi et al. [29] found that transoral laser microsurgery in treating T1 glottic cancer can effectively control local lesions and extend disease-free survival, with favorable cost-effectiveness.

This study has several limitations that need to be acknowledged. First, the relatively small sample size (n=80) and single-center retrospective design may have limited the generalizability of the findings. Future studies should conduct prospective, multi-center cohort studies to increase the representativeness of our findings. Second, the long-term prognosis of EGC patients was not evaluated. Extended follow-up periods of 3-5-year should be conducted to collect more information on prognosis, which can fill the relevant gaps. Finally, there is no robust investigation into factors influencing patient efficacy. Supplementary analysis in this regard can help formulate targeted intervention plans for greater efficacy.

### Conclusion

Compared to conventional laryngofissure, LTP-RFA provides better surgical outcomes, enhanced postoperative recovery, and higher curative

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efficacy for patients with early glottic carcinoma. In addition, it effectively alleviates postoperative pain, reduces MMP-9, NO, and VEGF levels, improves voice acoustic parameters and patient quality of life, and lowers postoperative complication rates.

### Disclosure of conflict of interest

None.

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