

# Comparison of Partial Laryngectomy Versus Radiotherapy for the Treatment of Early Glottic Carcinoma: Complications and Oncological Results: A Nonrandomized Clinical Trial

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Received: 12 Jun. 2021; Accepted: 20 Jan. 2022

**Abstract-** The aim of this non-randomized clinical trial was to evaluate tumor outcomes and subjective quality of voice following radiotherapy and partial laryngectomy in early-stage glottic laryngeal cancers. Non-Randomized Clinical Trial. Otolaryngology and radiation oncology clinics of Imam Khomeini (an affiliated hospital of Tehran University of Medical Sciences) and Amir Aalam Hospitals. Fifteen patients with early-stage glottic laryngeal carcinoma were admitted to the otolaryngology clinic, divided into two treatment groups: radiotherapy and partial laryngectomy. Of the total 50 patients, 25 had a partial laryngectomy and 25 radiotherapies. The comparison of the average of the Voice Handicap Index (VHI) showed significant improvement of vocal quality after treatment for both partial laryngectomy and radiotherapy ( $P < 0.0001$  for both). But there was no significant difference in VHI mean scores between the two treatment groups (patients treated by partial laryngectomy and radiotherapy). Short- and long-term complication was higher in patients undergoing surgery than radiotherapy group ( $P < 0.0001$ ). With regard to oncological outcome after one and eight-year after treatment, no differences were observed in the two treatment groups; there was a significant relationship between smoking cessation and recurrence of disease in the partial laryngectomy treatment group ( $P = 0.012$ ). There was no significant difference in voice quality and life expectancy of patients operated on using open surgery and patients treated with radiotherapy in this series. Open surgery may have more noticeable complications than radiotherapy.

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*Acta Med Iran* 2022;60(2):101-107.

**Keywords:** Partial laryngectomy; Radiotherapy; Early glottic carcinoma; Quality of voice; Voice handicap index; Complication

## Introduction

Laryngeal cancer, one of the common head and neck malignancies (1,2), is more common in Western Asia, the Caribbean, North and South America (3). Laryngeal cancer is also the most common head and neck region cancer in Iran (4), and over 40 % of the involved site is the larynx in various Iranian studies (1,4-6).

In 56-75% of cases, the disease is diagnosed in an early stage (T1 and T2), most frequently arising from the glottis (7). The goal of the treatment for early glottic

cancer is to cure the disease and increase the chance of survival while preserving the voice quality as well as minimal treatment complications.

Early-stage glottic carcinoma is treated with radiotherapy, carbon dioxide endoscopic laser surgery, or open partial laryngectomy with the intent to preserve laryngeal function (8). The selection of the best treatment depends on the location and stage of the tumor, the patient's comorbidity, the idea of the therapist, and the requests of the patient. Head and neck surgeons have notified those concerns about functional outcomes after

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## Partial laryngectomy vs radiotherapy in early glottic cancer

more extended resections still constitute an issue for many treating physicians, and it remains controversial which treatment is superior in voice preservation (9-12). A Cochrane review also has shown that “There is currently insufficient evidence to guide management decisions on the most effective treatment” (13). Overall, studies comparing treatment techniques have yielded conflicting results. One meta-analysis (14), one original study (15) and a review (16) did not find a significant difference in voice outcome between treatment modalities. On the other hand, Superior voice quality has been reported after Radiotherapy in several studies (11-12,17). A meta-analysis that was performed by Yoo *et al.*, (2013) recommended, for patients with early (T1) glottic cancer, treatment options include the equally effective choices of endolaryngeal surgery, with or without laser, and radiation therapy and the treatment modality selection should be based on patient and clinician preferences and general medical condition (18). There is no international consensus on preferred treatment, and, to our knowledge, no clinical trial exists to aid decision making.

Herein this nonrandomized clinical trial was to evaluate tumor outcomes, subjective quality of voice and complications following radiotherapy and partial laryngectomy in early stage (T1 and T2) glottic laryngeal carcinoma in a 5-year period.

## Materials and Methods

### Trial design

In a non-randomized prospective clinical trial study, patients with early stage (T1 and T2) laryngeal squamous cell carcinoma were allocated to radiotherapy or open surgery (partial laryngectomy) groups. Because of the ethical constraints, and special conditions of patients, random allocation was not possible. Therefore, non-randomized clinical study was conducted.

Intervention type was determined by the stage of the tumor, patient's comorbidity, and the patients' preference. This study was registered in Clinical Trials.gov registry with code number of NCT00497588. The patients were followed for 5-years after surgery or radiotherapy.

### Protocol approval

The protocol of this study was approved by the Institutional Review Board of the Tehran University of Medical Sciences. All aspects of the study were conducted according to the Declaration of Helsinki.

### Participants

Patients with T1-2, N0, M0 Squamous Cell Carcinoma of The Glottis (according to the 2002 International Union against Cancer classification system) were enrolled in this study (19). The exclusion criteria consisted of a history of any chronic respiratory conditions or cough, presence of any other benign lesion on the true vocal cords, history of phono surgery, history of radiotherapy, history of collagen vascular disorders, and vocal cord paralysis.

A total of 50 patients were enrolled in the clinical trial in a period (Figure 1). Twenty-five patients were treated with open partial laryngectomy, and 25 underwent radiation. Informed consent was obtained from all of the patients upon entering the study. The distribution of tumor stage, age, and smoking habits were evaluated in the two groups.

Each subject underwent an office-based rigid video laryngoscopy. Endoscopic examinations were conducted using either a Pentax FNL-10RP2 fiberscope or Wolf 4450.47 90° rigid telescope. Computed tomographic scans were done for every patient.

### Intervention

#### Radiotherapy

Radiotherapy was delivered to a total of 25 patients with a 6-MV photon linear accelerator. Patients were treated in a supine position using a thermoplastic immobilization mask. Target areas, including the larynx Standard field borders, were used in most cases as clinical target volume (CTV) for superior: mid thyroid notch; inferior: bottom of cricoid cartilage; posterior: 1 cm posterior to the thyroid cartilage but anterior to the vertebral body and 6 mm margin around CTV as planning target volume (PTV) generally using a standard parallel opposing technique for PTV coverage of 95% isodose curve and for more dose homogeneity; wedge compensators was used that no more than 107% isodose in PTV.

Patients with T1 laryngeal cancer were treated using 66 Gy in 2 Gy/fraction in 6.5 weeks and 70 Gy for T2 tumors in 7 weeks.

#### Partial laryngectomy

A total of 25 patients underwent a partial laryngectomy. Our criteria included the following: (1) the thyroid cartilage should not be invaded; (2) the arytenoid, except for the vocal process, should be free of tumor; (3) the supraglottic extension should extend no further than the lateral extension of the sinus of Morgagni; and (4) the recurrence should correlate with the primary tumor previously treated with Radiotherapy. In the surgery

group, supracricoid laryngectomy was performed on 12 patients (48%), while front lateral laryngectomy was used in 9 patients (36%), and cordectomy was used for the rest of the 4(16%).

### Voice quality follow up period

Follow up of voice quality was performed 12 months after cessation of treatment

### Voice evaluation

#### Voice handicap index

The duration of voice evaluation follow-up was 12 months from the end of the treatment. The patients completed the standard "Voice Handicap Index" (Henceforth VHI) via a self-evaluation form comprising 3 questions covering three domains. VHI is a widely used self-administered questionnaire with a Likert-type scale indicating how frequently each situation is experienced. The questionnaire has been translated and validated in previous studies (20).

Each question was assigned a score of 0-4 (from least disability to most). In each item, the scores were classified them as mild disability (less than 20), moderate (21-30) and severe (more than 30). The maximum score was 40 points. Adding the three scores together, the maximum possible was 120, So the vocal disability was classified as mild (less than 30), moderate (31-60), severe (61-90) and very severe (91-120) (21).

#### Complications follow-up

Short term complication consisted of tooth loss, trauma and hematoma (Coincide with intervention) and long-term complication (6 month from the end of the treatment) consisted of dry mouth, cough and hematoma

#### Recurrence and mortality follow- up

Recurrent disease and mortality follow-up was surveyed 5 years after treatment

### Statistical analysis

All analyses were by intention to treat. Patient voice quality was compared using the *t*-student test. All tests were two-sided and performed at a 5% significance level with 95% confidence intervals (CI). Internal validity was reinforced by confounding controlling.

### Results

#### Demographic and baseline data

Among 54 patients that were screened and admitted to Imam Khomeini and Amir-Aalam hospitals, overall, 50 eligible patients were finally enrolled in the Radiotherapy group partial laryngectomy group. In both treatment groups, all lesions corresponded to Stage I-II SCCG. None of the patients were professional voice users. Twenty-three patients (92%) in both groups were males.

In the surgery group, the range of ages was in 43-83 years, with a mean (SD) age of 60.16 (8.91). In the patient group treated with Radiotherapy, the ages were in the range 39-83 years, with an average age (SD) of 61.04 (10.48). No difference was observed in groups when comparing mean age ( $P>0.05$ ) and mean smoking pack/year ( $P>0.05$ ).

#### Voice handicap index results

The comparison of the average of VHI (at least 12 months after the operation or Radiotherapy) showed significant improvement of vocal quality after treatment for both partial laryngectomy and Radiotherapy (mean VHI before treatment; 58.88(31.0), after treatment; 12.04(4.96),  $P<0.0001$ ) and (mean VHI before treatment; 59.76(12.8), after treatment; 17.76(6.69)  $P<0.0001$ ) respectively, that a higher score ( $P\leq 0.05$ ) reflecting a worse outcome. There was no significant difference in VHI pooled (before minus after) mean scores in two treatment groups (patients treated by partial laryngectomy and radiotherapy (Table 1).

**Table 1. descriptive and analytical distribution of VHI among patients treated by Partial Laryngectomy and Radiotherapy**

Voice handicap index	Partial Laryngectomy		Radiotherapy	
	Before treatment	After treatment	Before treatment	After treatment
Mean (SD)	58.88 (31.0)	12.04 (4.96)	59.76 (12.8)	17.76 (6.69)
Median (Minimum-Maximum)	71.0 (10-116)	11.0 (8-25)	56.76 (44-94)	17.0 (10-36)
t- value ( <i>P</i> )*	9.56 (<0.0001)		14.54(<0.0001)	
t-value ( <i>P</i> )**	3.5(0.99)			

\*Two-sample paired *t*-test

\*\* Two-sample independent *t*-test

Voice evaluation was conducted at least 6 months after the operation or Radiotherapy. Voice evaluation average showed an overall superior outcome of subjective voice quality of voice in patients treated for both partial laryngectomy ( $t=-2.19, P<0.0001$ ) and Radiotherapy

( $t=1.59, P<0.0001$ ), There was no significant difference in voice evaluation pooled (before minus after) mean scores compared two treatment groups (patients treated by Radiotherapy and partial laryngectomy ( $t=1.03, P=0.3$ ) (Table 2).

**Table 2. Voice quality descriptive and analytical distribution among patients treated by Partial Laryngectomy and Radiotherapy**

	Partial Laryngectomy(n=25)		Radiotherapy(n=25)	
	Before treatment	After treatment	Before treatment	After treatment
<b>Voice quality, mean±SD (range)</b>	5.44±2.35(1.0-9.0)	6.88±2.3(1.0-10.0)	5.32±1.57(2.0-8.0)	6.08±1.8(2.09-9.0)
<b>t-value (P)*</b>	-2.19(=0.03)		-1.59(= 0.11)	
<b>t-value (P)**</b>	1.03(0.3)			

\*Two-sample paired *t*-test

\*\* Two-sample independent *t*-test

The short and long-term complication was higher in patients undergoing surgery than radiotherapy group ( $P<0.0001$ ) (Table 3).

While the complication was higher in patients undergoing surgery (20 cases), it should be noted that 4 cases of patients undergoing radiotherapy also had experienced complications. Long-term hematoma after

open partial laryngectomy (22 cases) was much more common than patients undergoing radiation therapy (4 cases). This study found one patient with respiratory pneumonia complication. Full evaluations of complications during treatment and functional results have presented in Table 3.

**Table 3. The complication and functional results distribution among patients treated by Partial Laryngectomy and radiotherapy**

Complications	Partial Laryngectomy	Radiotherapy	X <sup>2</sup> (P)
<b>With Short- Term Complications</b>	24(96.0)	12(48.0)	
<b>Respiratory Disorders</b>	1(4.17)	0(0.0)	
<b>Tooth loss</b>	0(0.0)	1(8.34)	
<b>Trauma</b>	20(83.33)	4(33.33)	14.29 (0.0001)
<b>Hematoma</b>	1(4.17)	0(0.0)	
<b>Trauma&amp; Hematoma</b>	2(8.33)	0(0.0)	
<b>Other*</b>	0(0.0)	7(58.33)	
<b>Without Short Term Complication</b>	1(4.0)	13(52.0)	
<b>Long Term Complication</b>	23(92.0)	9(36.0)	
<b>Dry mouth</b>	0(0.0)	3(33.33)	
<b>Cough</b>	0(0.0)	2(22.23)	
<b>Hematoma</b>	22(95.65)	4(44.44)	17.01 (0.0001)
<b>Other*</b>	1(4.35)	0(0.0)	
<b>Without Long Term Complication</b>	2 (8.0)	16(64.0)	

**Recurrence and mortality outcome**

Recurrent disease 8 years after treatment was observed in six patients (24 %) in the Laryngectomy surgery group and in five patients (20 %) in the Radiotherapy group. The mortality proportion in Laryngectomy surgery and Radiotherapy recurrence groups were four (66.66%) and three (60%) in recurrence cases, respectively (Table 4). Between the two groups (partial laryngectomy and Radiotherapy treatment), there

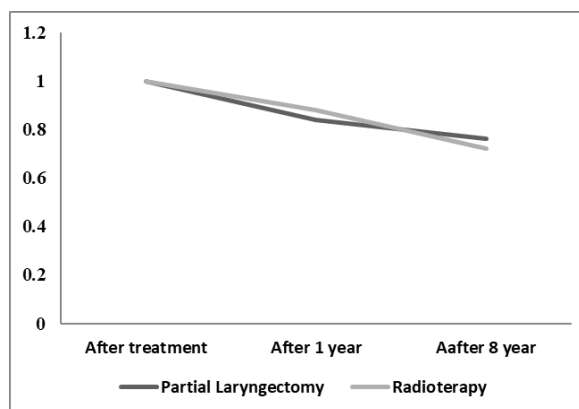
was no significant difference in recurrence ( $\chi^2=0.17, P=0.73$ ) and mortality ( $\chi^2=0.17, P=0.68$ ).

With regard to oncological outcome after one and 8 years after treatment, no differences were observed in the two treatment groups, as shown in Figure 1

It's noticeable; there was a significant relationship between smoking cessation and recurrence of disease in the partial laryngectomy treatment group ( $P=0.012$ ).

**Table 4. Descriptive distribution of oncology outcome in treatment groups**

Recurrence after intervention frequency (%)		Treatment type after recurrence			mortality after recurrence			
Partial Laryngectomy (n=25)	Radiotherapy (n=25)	Chemotherapy	surgery	Chemotherapy	surgery	Partial Laryngectomy	Radiotherapy	
(n=50)	6(24)	5(20)	3(12)	3(12)	5(20)	0(0.0)	4(16)	3(12)

**Figure 1.** Overall survival in partial laryngectomy and radiotherapy groups

## Discussion

One of the main expectation of most patients with early laryngeal cancer is having a good voice with a completely controlled disease. However, the priority of none of the routine treatments is well-established. In this study, there was no significant difference in the voice quality of patients between the two groups ( $P>0.05$ ). The voice impairment for patients after Radiotherapy for early glottic cancer was studied in some studies (22-24) and has reported conflicting results. Inconsistency of our study, Arias (2013) concluded that the voice characteristics of patients diagnosed with early glottis cancer improved after radiotherapy of their patients in Spain (10).

In Milovanović and coauthors' study (2009), the voice quality was much better after laser cordectomy compared to open surgery; however, the functional results of voice quality, after a laser cordectomy, were worse when compared to the group of patients treated with radiotherapy. They determined that there was no crucial difference in the voice quality of patients operated using laser cordectomy and patients primarily treated with radiotherapy and these two methods were superior to open surgery cordectomy (22). In 2010, a Cochrane review was published that compared radiotherapy versus

surgery (with or without laser) for early laryngeal squamous cell cancer. Only 1 randomized controlled trial was identified that compared open surgery and radiotherapy among a substantial number of patients with early glottic laryngeal cancer, and the authors concluded that there is currently insufficient evidence to guide management decisions on the most effective treatment (13). Performing randomized controlled trials comparing open surgery and radiotherapy in patients with early glottic cancer is limited. The selection of treatment type is dependent on the location and stage of the tumor and the patient's comorbidity and preference.

Regarding the complications, some studies have shown that partial laryngectomy promotes better results concerning dental problems and dry mouth, which is consistent with our study (8,25). In total, it has been found that partial laryngectomy is responsible for the higher incidence of these short and long undesirable effects when compared to radiation therapy ( $P=0.0001$ ).

In our study, no differences were observed in 5-year survival rates between two treatment groups. Overall, there are reports suggesting that five-year survival rates open partial laryngectomy and after radiotherapy are the same on patients with glottic cancer (26). For example, it was calculated 72.9% and 77.4% after surgery and

radiotherapy, respectively, in Graciano's study (8). A similar result was observed in the present study, with five-year survival rates of 76.0 and 72.0% after surgery and Radiotherapy, respectively. Since the probability of equivalent oncological outcomes, some specialist recommends that partial laryngectomy should be considered as the main therapeutic selection for glottic tumors because it determines a precise pathological staging of the disease (27).

However, radiotherapy has presented the primary technique of initial treatment for glottic carcinoma in most centers. The prevalence of radiotherapy treatment was calculated, 84.4% and 63.2% in patients of Canada and the United States (28). It is obvious that radiotherapy avoids tracheostomy, usually associated with a conservative laryngectomy. But it is interesting that definitive tracheostomy rates (tracheostomy after initial treatment) were calculated, 28.1% and 23.3% after radiotherapy and open partial laryngectomy, respectively (8).

In concordance with some studies, one of the related factors that adversely influence voice quality was smoking after the completed treatment in our study (29-30).

This report is among few studies compared two famous treatment modalities of early laryngeal cancers. However, it has some limitations as well. The main limitation of this study was high probability of allocation bias, because of lack of randomization. Despite the initial design of this study our Ethical committee did not give us permission of randomization.

Albeit, we controlled common confounding variables such as age, gender, comorbidity of disease and smoking habit. Also, VHI is a subjective tool, which has its own downsides. We propose future studies with objective tools for better comparison. Finally, larger series need to confirm the main outcome of this study.

Partial laryngectomy and radiotherapy may have comparable results in voice quality and life expectancy of early laryngeal cancer patients.

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