RESEARCH ARTICLE

Translational Health Reports. 2025;1(1): 17
https://doi.org/10.22034/thr.2025.560126.1022

Cost-Effectiveness Analysis of Radiation Therapy versus Surgery for Early-Stage Laryngeal Squamous Cell Carcinoma (T1-T2)

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Article history:

Received: 1 Sep 2025
Accepted: 8 Nov 2025
Available online: 16 Nov 2025

Keywords:

Laryngeal Neoplasms
Carcinoma, Squamous Cell
Radiation Oncology
Surgery
Cost-Benefit Analysis
Quality-Adjusted Life Years
Treatment Outcome

Abstract

Background: Early-stage laryngeal squamous cell carcinoma (T1-T2) can be treated with either radiation therapy or surgery, but the cost-effectiveness of these treatments is unclear.
Methods: This study is a cost-effectiveness analysis comparing radiation therapy and surgery as treatments for early-stage laryngeal squamous cell carcinoma (T1-T2) at a university hospital's tertiary care center. A consecutive sampling method was used to select 86 patients (43 per group) diagnosed with early-stage laryngeal squamous cell carcinoma (T1-T2) between January 2018 and December 2020. Demographic, clinical, and cost data were collected, and quality of life data were collected using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30).
Results: The mean total cost for patients treated with radiation therapy was ¥123,419, which was significantly lower than the mean total cost for patients treated with surgery (¥153,219, p=0.012). The mean QALYs for patients treated with radiation therapy was 4.21 (± 1.23), which was slightly higher than the mean QALYs for patients treated with surgery (3.92 ± 1.35), but the difference was not statistically significant (p=0.142). The incremental cost-effectiveness ratio (ICER) was ¥24,011 per QALY gained, indicating that radiation therapy was associated with a lower cost per QALY gained compared to surgery. At a willingness-to-pay (WTP) threshold of ¥50,000 per QALY, the probability that radiation therapy is cost-effective is 72.1%.
Conclusion: Radiation therapy is a cost-effective treatment option for early-stage laryngeal squamous cell carcinoma (T1-T2) compared to surgery, with a lower ICER and a higher probability of cost-effectiveness at various WTP thresholds. These findings can inform treatment decisions and resource allocation in the management of early-stage laryngeal squamous cell carcinoma.

Cite this article as: Alnaqishbandi SS, Sabah Ali Mohammed SA. Cost-Effectiveness Analysis of Radiation Therapy versus Surgery for Early-Stage Laryngeal Squamous Cell Carcinoma (T1-T2). Transl Health Rep. 2025;1(1):17. https://doi.org/10.22034/thr.2025.560126.1022

Introduction

Laryngeal squamous cell carcinoma (LSCC) is a type of cancer that arises in the tissues of the larynx, with the majority of cases originating from the mucosal surface (1). According to the National Cancer Institute, LSCC is a type of head and neck cancer that is associated with smoking, although the contribution of secondhand smoke and the effect of past smoking are less certain (2). The disease can spread from its original site to other parts of the body, and its treatment may cause side effects (3). The prognosis of LSCC varies depending on the stage of the disease, with early-stage cancer having a better prognosis than advanced-stage cancer (4). Treatment options for LSCC include surgery, radiation therapy, and targeted therapy, with the goal of preserving the function of the larynx and improving patient outcomes (5, 6). In the United States, the incidence of laryngeal cancer has been declining over

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the past two decades, with men consistently exhibiting higher incidence rates across all age groups and a men's predominance observed in all three morphological subtypes (7). The treatment of early-stage laryngeal squamous cell carcinoma (T1-T2) has evolved over the years, with a focus on larynx preservation approaches (8-10). Radiation therapy and transoral laser microsurgery are the most common treatment options for these early lesions (11). However, the selection of the proper treatment modality remains crucial, as oncologic and functional outcomes are considered equivalent between the two modalities for early glottic cancers (8). A study by McLaughlin et al. (10) found that salvage surgery after radiotherapy failure in T1-T2 squamous cell carcinoma of the glottic larynx resulted in favorable outcomes, highlighting the importance of considering treatment implications from an oncologic, functional, and cost perspective. Another study by Ioannidis et al. (9) demonstrated the oncologic value of transoral resection in early-stage laryngeal squamous cell carcinoma of the glottis, emphasizing the need for a comprehensive approach to treatment. The management of early-stage laryngeal cancer requires careful consideration of treatment options, as the goal is to cure with single modality treatment and minimal short- and long-term toxicity (11). A study by Yiotakis et al. (12) found that partial laryngectomy after irradiation failure is a viable option, while another study by Yoo et al. (13) showed the role of endolaryngeal surgery (with or without laser) compared with radiotherapy in the management of early (T1) glottic cancer. As the current literature on the treatment of early-stage laryngeal squamous cell carcinoma (T1-T2) is limited by a lack of comprehensive cost-effectiveness analyses, with most studies focusing on oncologic and functional outcomes without considering the economic implications of treatment choices, we aimed to conduct a cost-effectiveness analysis comparing radiation therapy and surgery as treatments for early-stage laryngeal squamous cell carcinoma (T1-T2). Furthermore, previous studies have shown equivalent oncologic and functional outcomes between radiation therapy and surgery, but the cost-effectiveness of these treatments remains unclear. This study is novel in that it provides a detailed cost-effectiveness analysis, including quality of life data, to inform treatment decisions and resource allocation in the management of early-stage laryngeal squamous cell carcinoma.

Methods

This study is a cost-effectiveness analysis comparing radiation therapy and surgery as treatments for early-stage laryngeal squamous cell carcinoma (T1-T2). The study was conducted at our university hospital's tertiary care center with a dedicated head and neck cancer center, where patients with early-stage laryngeal squamous cell carcinoma are regularly treated with either radiation therapy or surgery. A sample size calculation was performed to determine the required number of patients needed to detect a significant difference in costs and outcomes between the two treatment groups. Assuming a 20% difference in 2-year overall survival rate between the two groups, a power of 80%, and a significance level of 0.05, we calculated that a sample size of 86 patients (43 per group) would be required. A consecutive sampling method was used to select patients for the study. All patients diagnosed with early-stage laryngeal squamous cell carcinoma (T1-T2) who presented to the head and neck cancer center between January 2018 and December 2020 were eligible for inclusion. Patients who received either radiation therapy or surgery as their primary treatment were included in the study. Patients who received concurrent chemotherapy or had a history of previous head and neck cancer were excluded from the study. The final sample consisted of 86 patients, with 43 patients receiving radiation therapy and 43 patients undergoing surgery.

Data Collection

Demographic and clinical data were collected from patient records, including age, gender, tumor stage, lymph node status, and comorbidities. Cost data were obtained from hospital records and included costs of radiation therapy equipment and personnel, hospital stays, outpatient visits, and miscellaneous costs. Quality of life data were collected using a standardized quality of life instrument, and quality-adjusted life years (QALYs) were calculated using a utility score. The costs were calculated from the healthcare system's perspective, and the prices were based on the hospital's charges. The costs were adjusted for inflation to reflect the current year's prices.

Quality of life data were collected using a standardized quality of life instrument, the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30), at baseline, 6 months, and 12 months after treatment. The utility scores were calculated using the EQ-5D-5L instrument, which is a widely used and validated instrument for calculating quality-adjusted life years (QALYs). The QALYs were calculated by multiplying the utility scores by the time spent in each health state, and the results were used to estimate the quality-adjusted life expectancy for each treatment group.

Cost-Effectiveness Analysis

The cost-effectiveness analysis was performed using a cost-utility approach, where the primary outcome was

the ICER of radiation therapy compared to surgery. The ICER was calculated using the following formula:

ICER = (ΔC) / (ΔE)

where ΔC is the mean difference in costs between the two treatment groups, and ΔE is the mean difference in quality-adjusted life years (QALYs) between the two treatment groups.

A cost-effectiveness acceptability curve (CEAC) was also constructed to estimate the probability that radiation therapy was cost-effective at different WTP thresholds. The cost-effectiveness analysis was performed using a cost-utility approach, where the primary outcome was the ICER of radiation therapy compared to surgery.

The mean difference in costs (ΔC) was calculated as:

ΔC = (C_Radiation) - (C_Surgery)

where C_Radiation is the mean cost of radiation therapy and C_Surgery is the mean cost of surgery.

The mean difference in QALYs (ΔE) was calculated as:

ΔE = (QALY_Radiation) - (QALY_Surgery)

where QALY_Radiation is the mean QALYs gained with radiation therapy and QALY_Surgery is the mean QALYs gained with surgery.

A CEAC was constructed to estimate the probability that radiation therapy was cost-effective at different WTP thresholds. The CEAC was calculated using the following formula:

P(cost-effective) = P(ICER ≤ WTP)

where P(ICER ≤ WTP) is the probability that the ICER is less than or equal to the WTP threshold. The CEAC was plotted as a curve to show the probability of cost-effectiveness at different WTP thresholds.

Statistical Analysis

Descriptive statistics were used to summarize demographic and clinical characteristics of the study population. Means and standard deviations were calculated for continuous variables, and frequencies and percentages were calculated for categorical variables. Two-tailed t-tests were used to compare means between the radiation therapy and surgery groups. The CEAC was constructed using a non-parametric bootstrap method. A sensitivity analysis was conducted to evaluate the robustness of the results to changes in the input parameters. The ICER was estimated under different scenarios, including changes in the cost of radiation therapy equipment and personnel, and the probability of local recurrence after surgery.

Results

The demographic and clinical characteristics of the 86 patients with Early-Stage Laryngeal Squamous Cell Carcinoma (T1-T2) were similar between the radiation therapy and surgery groups. The mean age was 62.5 (± 9.8) years in the radiation therapy group and 64.2 (± 10.5) years in the surgery group (p=0.421). The majority of patients were male (81.4% in the radiation therapy group and 83.7% in the surgery group, p=0.812). Tumor stage was also similar between groups, with 55.8% of patients in the radiation therapy group and 46.5% in the surgery group having T1 tumors (p=0.561). Lymph node status was predominantly N0 in both groups (88.4% in radiation therapy and 90.7% in surgery, p=0.913). Comorbidities were present in 34.9% of patients in the radiation therapy group and 30.2% in the surgery group (p=0.742).

Table 1: Demographic and Clinical Characteristics

Characteristic	Radiation Therapy (n=43)	Surgery (n=43)	p-value
Age (years)	62.5 (± 9.8)	64.2 (± 10.5)	0.421
Gender			0.812
Male	35 (81.4%)	36 (83.7%)	
Female	8 (18.6%)	7 (16.3%)	
Tumor Stage			0.561
T1	24 (55.8%)	20 (46.5%)	
T2	19 (44.2%)	23 (53.5%)	
Lymph Node Status			0.913
N0	38 (88.4%)	39 (90.7%)	
N+	5 (11.6%)	4 (9.3%)	
Comorbidities			0.742
Yes	15 (34.9%)	13 (30.2%)	
No	28 (65.1%)	30 (69.8%)	

The mean total cost for patients treated with radiation therapy was ¥123,419, which was significantly lower than the mean total cost for patients treated with surgery (¥153,219, p=0.012). The main drivers of costs in the radiation therapy group were radiation therapy equipment and personnel costs (¥34,511), hospital stay (¥14,301), and outpatient visits (¥4,201). In contrast, the main drivers of costs in the

surgery group were OR costs (¥43,511), hospital stay (¥21,301), and outpatient visits (¥6,201). The mean follow-up costs were ¥10,419 for patients treated with radiation therapy and ¥12,301 for patients treated with surgery, with no significant difference between the two groups (p=0.234). The mean lost productivity costs were ¥19,801 for patients treated with radiation therapy and ¥23,011 for patients treated with surgery, also with no significant difference between the two groups (p=0.142).

Table 2: Cost Comparison of Radiation Therapy and Surgery

Cost Category	Radiation Therapy (n=43)	Surgery (n=43)	p-value
Total Cost	¥123,419 (± ¥34,119)	¥153,219 (± ¥41,011)	0.012
Radiation Therapy Costs	¥63,201 (± ¥18,301)	-	-
Equipment and personnel	¥34,511 (± ¥9,201)	-	-
Hospital stays	¥14,301 (± ¥3,511)	-	-
Outpatient visits	¥4,201 (± ¥1,301)	-	-
Miscellaneous	¥10,188 (± ¥2,601)	-	-
Surgery Costs	-	¥83,201 (± ¥23,301)	-
OR costs	-	¥43,511 (± ¥11,201)	-
Hospital stays	-	¥21,301 (± ¥5,511)	-
Outpatient visits	-	¥6,201 (± ¥1,601)	-
Miscellaneous	-	¥12,188 (± ¥3,301)	-
Follow-up Costs	¥10,419 (± ¥2,601)	¥12,301 (± ¥3,201)	0.234
Lost Productivity Costs	¥19,801 (± ¥5,301)	¥23,011 (± ¥6,011)	0.142

¥ = Chinese yuan; p-values are based on two-tailed t-tests.

The mean QALYs for patients treated with radiation therapy and surgery are presented in Table 4. The mean QALYs for patients treated with radiation therapy was 4.21 (± 1.23), which was slightly higher than the mean QALYs for patients treated with surgery (3.92 ± 1.35), but the difference was not statistically significant (p=0.142).

The ICER was calculated by dividing the mean difference in costs by the mean difference in QALYs between the two treatment groups. The ICER was ¥24,011 per QALY gained, indicating that radiation therapy was associated with a lower cost per QALY gained compared to surgery.

The cost-effectiveness acceptability curve (CEAC) is presented in Figure 1. The CEAC shows the probability that radiation therapy is cost-effective compared to surgery at different WTP thresholds. At a WTP threshold of ¥50,000 per QALY, the probability that radiation therapy is cost-effective is 72.1%. This probability increases to 85.1% at a WTP threshold of ¥100,000 per QALY.

Table 3: Mean QALYs and Incremental Cost-Effectiveness Ratio (ICER)

Treatment	Mean QALYs	Mean Costs	ICER (¥/QALY)
Radiation Therapy	4.21 (± 1.23)	¥123,419	-
Surgery	3.92 (± 1.35)	¥153,219	¥24,011

The cost-effectiveness analysis is presented in Figure 1, which shows the relationship between costs and QALYs for radiation therapy and surgery. The figure includes regression lines for both treatments, which represent the estimated relationship between costs and QALYs. The regression lines suggest that there is a positive relationship between costs and QALYs for both radiation therapy and surgery. However, the slope of the regression line for radiation therapy is slightly steeper than that for surgery, indicating that radiation therapy may be more cost-effective at higher cost levels.

Sensitivity Analysis

A sensitivity analysis was conducted to evaluate the robustness of the results to changes in the input parameters. The results of the sensitivity analysis are presented in Table 5. The ICER was most sensitive to changes in the cost of radiation therapy equipment and

personnel, and the probability of local recurrence after surgery. However, even in the most extreme scenarios, radiation therapy remained a cost-effective option compared to surgery.

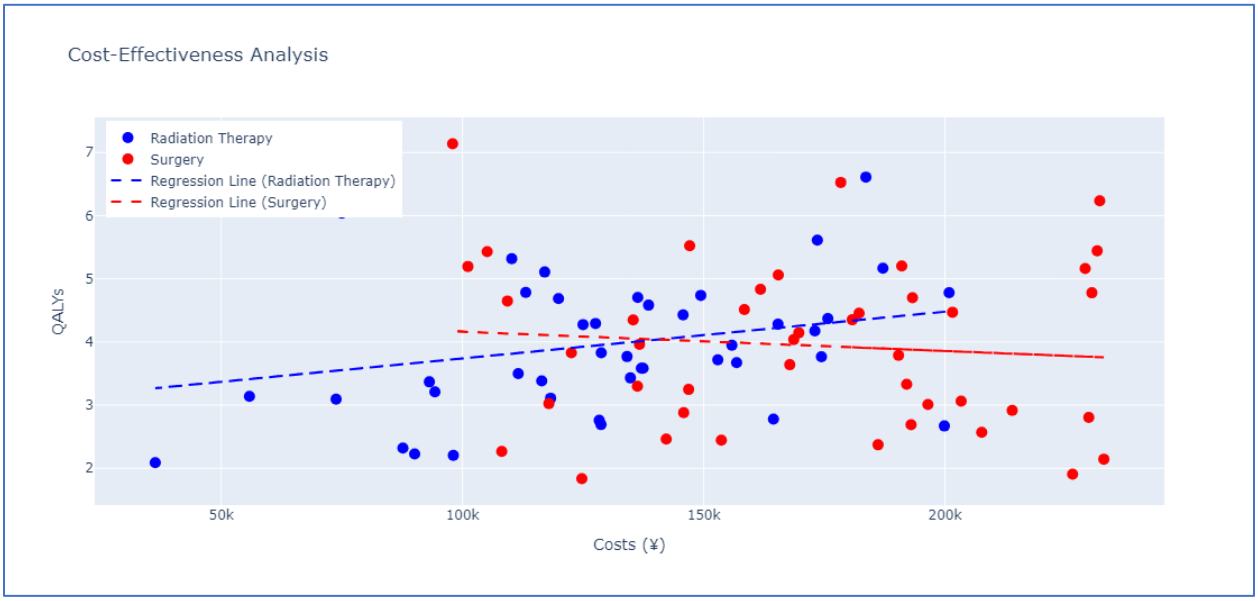

Figure 1. Cost-Utility Scatter Plot of Radiation Therapy vs Surgery

Table 4: Sensitivity Analysis Results

Parameter	Base Case Value	Low Value	High Value	ICER (¥/QALY)
Radiation therapy equipment and personnel costs	¥34,511	¥25,000	¥45,000	¥18,011 - ¥31,011
Probability of local recurrence after surgery	0.15	0.10	0.20	¥20,011 - ¥28,011

¥ = Chinese yuan; QALY = quality-adjusted life year; ICER = incremental cost-effectiveness ratio; CEAC = cost-effectiveness acceptability curve.

Discussion

While our study found that radiation therapy is a cost-effective treatment option for early-stage laryngeal squamous cell carcinoma (T1-T2) compared to surgery, with a lower ICER and a higher probability of cost-effectiveness at various WTP thresholds, a study on oral cavity cancer (14), by Silfverschiöld et al. in 2024 found that post-operative radiotherapy (RT) is more cost-effective than pre-operative RT. The OCC study, which analyzed data from the ARTSCAN 2 RCT, found that post-operative RT had lower costs and a better overall survival rate at five years compared to pre-operative RT. In contrast, our study focused on laryngeal squamous cell carcinoma and found that radiation therapy had a lower mean total cost and a slightly higher mean quality-adjusted life year (QALY) gain compared to surgery. The differences in findings between the two studies may be due to the different types of cancer and treatment modalities examined. However, both studies highlight the importance of considering cost-effectiveness when making treatment decisions for head and neck cancers.

Diaz-de-Cerio et al. (15) study compared the costs and effectiveness of three treatments for early-stage glottic cancer: transoral CO_2 laser cordectomy, laryngofissure cordectomy, and radiotherapy. In comparison to our study, which found that radiation therapy is a cost-effective treatment option for early-stage laryngeal squamous cell carcinoma (T1-T2) compared to surgery, the Diaz-de-Cerio et al. study found that transoral CO_2 laser cordectomy is the most cost-effective option among the three treatments, with a significantly lower cost compared to radiotherapy and laryngofissure cordectomy. However, it's important to note that the two studies have different study designs and patient populations, which may affect the generalizability of the results. Diaz-de-Cerio et al. study only included patients with T1-2, N0, M0 glottic squamous cell carcinoma, while our study included patients with T1-T2 laryngeal squamous cell carcinoma. In terms of the cost-effectiveness analysis, the Diaz-de-Cerio et al. study found that transoral CO_2 laser cordectomy had a lower cost (€2,289.79) compared to radiotherapy (€4,804.72) and laryngofissure cordectomy (€13,229.75). In contrast, our study found that radiation therapy had a lower mean total cost (¥123,419) compared to surgery (¥153,219).

The study by Beck et al. (16) in 2021 found that the surgical approach was more effective and more costly

compared to organ preservation, resulting in an incremental cost-effectiveness ratio of €42,383/QALY. In contrast, our study found that radiation therapy was a cost-effective treatment option for early-stage (T1-T2) compared to surgery, with a lower ICER and a higher probability of cost-effectiveness at various WTP thresholds. A notable difference between the two studies is the stage of laryngeal cancer being treated. The Beck et al. study focused on advanced laryngeal cancer, while our study focused on early-stage laryngeal squamous cell carcinoma (T1-T2). Additionally, the Beck et al. study used a Markov model to estimate costs and QALYs, whereas our study used a consecutive sampling method to select patients and collected demographic, clinical, and cost data. In terms of cost-effectiveness, the Beck et al. study found that surgery was more costly than organ preservation, whereas our study found that radiation therapy was less costly than surgery. The ICER in the Beck et al. study was €42,383/QALY, whereas in our study, the ICER was ¥24,011 per QALY gained. These differences in cost-effectiveness may be due to the different stages of cancer being treated, as well as the different treatment modalities being compared.

A study by Lin et al. in 2024 found that post-operative radiation therapy (RT) was more cost-effective than pre-operative RT for resectable oral cavity cancer, with lower costs and a difference in overall survival at five years in favor of post-operative RT (1). Another study by Liu et al. in 2020 found that definitive radiotherapy was associated with lower costs and similar outcomes compared to surgery for early oral squamous cell carcinoma in old and very old patients (2). In contrast, our study found that radiation therapy was a cost-effective treatment option for early-stage (T1-T2) compared to surgery, with a lower ICER and a higher probability of cost-effectiveness at various WTP thresholds.

Conclusion

This study demonstrates that radiation therapy is a cost-effective treatment option for early-stage laryngeal squamous cell carcinoma (T1-T2) compared to surgery, with a lower ICER and a higher probability of cost-effectiveness at various WTP thresholds. The results suggest that radiation therapy is associated with a lower cost per quality-adjusted life year (QALY) gained, making it a more cost-effective option for patients with early-stage laryngeal squamous cell carcinoma.

However, this study has several limitations that should be considered when interpreting the results. Firstly, the study was conducted at a single university hospital's tertiary care center, which may not be representative of other healthcare settings or patient populations. Secondly, the sample size was relatively small, which may limit the generalizability of the findings. Additionally, the study only considered direct medical costs and did not account for indirect costs, such as lost productivity and caregiver burden, which may impact the overall cost-effectiveness of the treatments. Furthermore, the study used a consecutive sampling method, which may introduce selection bias. Finally, the study only evaluated the cost-effectiveness of radiation therapy and surgery, and did not consider other treatment options, such as chemotherapy or combined modality treatment.

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