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Article

Effect of Surgery on Prognosis of Laryngeal Cancer Patients and Its Influencing Factors: A Retrospective Study Based on Seer Database

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Abstract

Background: Currently, the primary treatment modality for laryngeal cancer (LC) is surgery. However, there is almost no evidence on the effectiveness of surgical resection in the prognosis of laryngeal cancer patients. Furthermore, the prognostic factors influencing outcomes in patients undergoing surgery for laryngeal cancer remain largely unexplored and poorly understood.

Methods: In this study, 59,873 patients with laryngeal tumors from 2000 to 2021 in the Surveillance, Epidemiology, and End Results (SEER) database were analyzed retrospectively. First, we applied propensity score matching (PSM) to construct a balanced cohort with and without surgery by 1:1 pairing with 0.2 standard deviation. After that, Kaplan-Meier analysis and multivariate Cox regression analysis were conducted to assess the therapeutic effect of surgery on patients and we used overall survival (OS) and laryngeal cancer-specific survival (LCSS) to measure it. The two groups were compared by constructing Fine-Gray competitive risk model. The nomogram prediction model of OS and LCSS in patients undergoing LC surgery was established by R software. Finally, the feasibility of the model was verified by calibration curve and consistency index (C-index).

Results: A total of 12,283 eligible patients were screened out, and 6,446 (52.4%) patients among it have received surgery. 7393 patients were successfully matched by PSM, and there was roughly a balance between the groups. In the matched data set, multivariate Cox analysis shows that surgery can reduce the risk of OS by 35.9%(HR=0.641, 95%CI 0.606 to 0.677) and the risk of LCSS by 41.5%(HR=0.585, 95%CI 0.533 to 0.641). The competitive risk model also shows that surgery can reduce the risk of patients. In addition, the nomogram model indicates that the surgical patients with radiotherapy can benefit more from surgery, while the patients with chemotherapy may be negatively affected.Finally, the 1-year, 5-year and 10-year survival rates of patients are intuitively visualized.

Conclusion: This study provides evidence that surgery can improve the prognosis of patients with laryngeal cancer, especially the subgroup of patients with glottic tumors and radiotherapy.

1. Introduction

As one of the most prevalent head and neck malignant tumors, there are more than 184,000 new cases of Laryngeal cancer worldwide every year [1,2] LC accounts for approximately 20% of head and neck malignant tumors, and is the second largest tumor of the upper gastrointestinal tract [3]. The incidence of laryngeal cancer is much higher in males compared to females, with smoking, alcohol consumption, and HPV and EBV virus infections being key risk factors closely associated with its development [4]. At present, Emerging research also suggests that human papillomavirus (HPV) may contribute to the pathogenesis of a subset of laryngeal cancers [5,6]. Common clinical manifestations of laryngeal cancer include hoarseness, dyspnea, and dysphagia. Besides, recent studies have shown that head and neck tumors, especially laryngeal cancer, can promote the development of obstructive sleep apnea syndrome (OSA) by altering the anatomical structure of the upper airway [7]. Squamous cell carcinoma (SCC) is the most frequently diagnosed histological subtype, accounting for an estimated 85%-95% of all laryngeal cancers [8]. Laryngeal cancer is classified intoprimary and secondary cancer. Primary Primary laryngeal carcinoma originates in the larynx, with squamous cell carcinoma being the predominant type. Secondary laryngeal carcinoma refers to the metastasis of malignant tumor from other sites to the larynx, which is relatively rare. Primary laryngeal cancer accounts for 95% to 99% of all laryngeal cancers. This study focuses on primary laryngeal cancer.

The incidence of laryngeal cancer is generally declining, but this is less pronounced in women and young subjects. Some countries and regions, such as Japan, Switzerland, and the Czech Republic, even show an increase in female morbidity and the average annual percentage change (AAPC) was 6.01, 5.61 and 3.31, respectively [9]. Globally, the age-standardized incidence of laryngeal cancer (ASIR) averaged an annual average growth rate (EAPC) from 1990 to 2017 of -0. 99 [10]. Although the incidence and mortality rates of throat cancer are decreasing, Laryngeal cancer represents a substantial burden in terms of global morbidity and mortality [11]. Because of the important physiological function of the larynx, advanced laryngeal cancer patients have high incidence rate and mortality, contributing to increased healthcare costs and economic strain on society [12,13]. The latest global analysis of laryngeal cancer shows that the age standardized rate (ASR) of incidence rate and mortality of laryngeal cancer worldwide is 2.0 and 1.0 per 100000 people, respectively. A recent study with the theme of the survival trend of LC showed that the relative survival rate and overall survival rate of 2 years and 5 years had little improvement, which highlighted the necessity of further study on LC survival rate [14,15].

Traditional treatments for laryngeal cancer include surgery, radiotherapy and chemotherapy, which can be used alone or in combination. In the early stage of disease, laryngectomy or local radiotherapy alone is usually used for successful treatment, the comprehensive treatment that includes total laryngectomy combined with adjuvant radiotherapy and chemotherapy is the main treatment method [6]. Adjuvant radiotherapy after total laryngectomy has been widely regarded as the standard management scheme for many years [16].

In addition to traditional surgical treatment, radiotherapy, and chemotherapy, the development of modern medicine has provided increasingly diverse treatment methods, such as immunotherapy, targeted therapy, and so on. Immunotherapy uses the human immune system to combat various malignant tumors, promoting changes in traditional treatment methods [17]. Studies have shown that low-level stromal tumor infiltrating lymphocytes (TIL) are closely associated with the recurrence of advanced laryngeal cancer [18], suggesting that immunotherapy may be effective in treating laryngeal cancer. Besides, autophagy and circular RNA (circRNA) play a certain role in the progression and chemotherapy resistance of laryngeal squamous cell carcinoma [19,20], providing new ideas for targeted therapy of laryngeal cancer in the future.

Despite the central role of surgery in the treatment of LC, it's precise impact on patient prognosis remains unclear. and there is no literature to study the factors influencing the prognosis of laryngeal cancer patients undergoing surgery. Current analyses are predominantly limited to small-scale case reports and case series, with a scarcity of large, population-based studies. This limitation hampers significant advancements in understanding the incidence and survival trends of laryngeal cancer. Therefore, this study uses SEER database to assess the role of surgery on the prognosis of LC patients. Additionally, in this population-based retrospective study, we developed a predictive model for post-surgical survival in laryngeal cancer patients, with the aim of informing clinical decision-making and guiding future research.

2. Method

2.1 Data Sources and Patients Selection

This research utilizes the SEER database (www.seer.cancer.gov) published in November 2023. The study population were extracted from SEER*Stat Version 8.4.3. which contains population-based data from 17 cancer registries, covering about 26.5% of the cancer population in the US from 2000 to 2021 (based on the 2020 population census). The SEER database provides details of the patient's tumor characteristics, diagnosis and treatment [2]. This study extracted the data of patients with laryngeal cancer from January 2000 to November 2021, including surgical records.

We included patients diagnosed with LC in the United States from 2000 to 2021, with follow-up extending untildeath or the end of the specified follow-up time. During this period, a total of 59,873 cases of laryngeal cancer were recorded in the SEER database. The inclusion criteria were as follows: laryngeal tumors (including glottis, supraglottis, subglottic, larynx, etc.); Exclusion criteria were as follows: (1) Ethnic information is unknown; (2) The grade information is unknown; (3) The tumor size information is unknown; (4) The follow-up or survival time is unknown; (5) Other necessary information (such as T, N and M stage) is blank. Finally, 12283 eligible patients were collected for analysis (Figure 1).

Due to SEER being a public and open database, the identity of the data used is unknown, therefore this study is exempt from review by the ethics review committee and does not require informed consent.

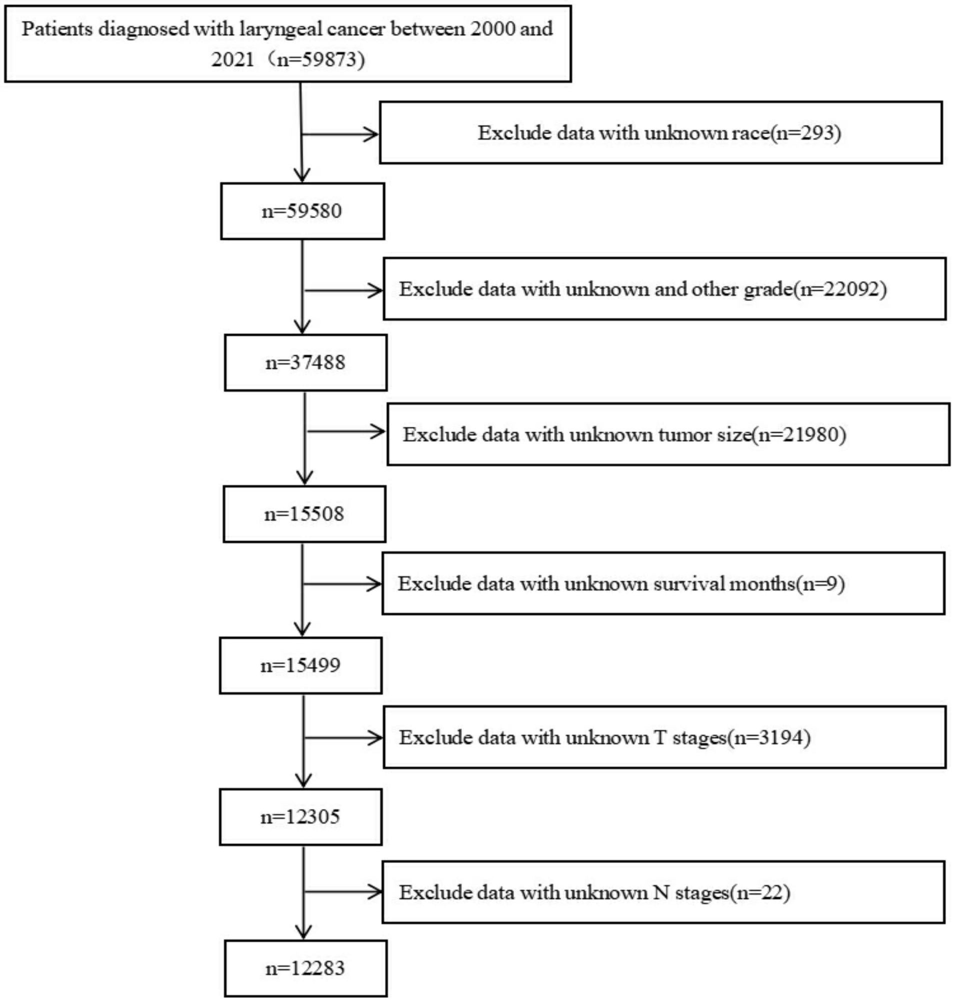

Figure 1. Seer data screening flow chart

2.2 Data Analysis

In this study, the OS and LCSS were used as the research outcomes. OS is defined as the time from the time of diagnosis to death due to various causes, and in the case of death, the time from diagnosis to the last follow-up record. LCSS is defined as the time from diagnosis to death attributable to laryngeal cancer. The description of "COD to site rec KM" from seer defines the cause of death.

Firstly, the data were preprocessed and the variables were classified. Age is divided into three groups (< 50 years old, 50-79 years old and > 80 years old). Other races except black and white are classified as “other” groups. We constructed a baseline table to compare the characteristics of patients and apply different tests according to different variables. Mean and standard deviation are used to measure the tumor size and survival time of patients. To address potential baseline imbalances between the surgical and non-surgical patients, propensity score matching (PSM) was utilized to excluded the interference of confounding variables.. A logit regression model was employed to evaluate each patient’s scores, using surgery status (performed or not performed) as the categorical variable. Covariates were age group, race, gender, marital status, T/N/M stage, tumor grade (gradin based on histology), distant metastasis, tumor size, location, chemotherapy, and radiotherapy status. The MatchIt package in R software was used for 1:1 matching between two groups, with the caliper width set to 0.2...P value<0.05 demonstrating the balance of characteristics between groups after PSM, which is consistent with the meaning of SMD <0.1. K-M curve shows the survival rate at different time points. The survival outcomes, including OS and LCSS, were compared between patients with or without surgery. After that, we a constructed a multivariate Cox regression model estimated the impact of surgery, age, race, marriage, gender, tumor site, T/N/M stage, grade, metastasis, radiotherapy and chemotherapy. The hazard ratio (HR) was calculated to evaluate the role of surgical treatment for LC patients. When competitive risk events are present in the data, the Fine-Gray competing risk model provides a more accurate analysis of survival outcomes than Kaplan-Meier curve analysis and the traditional Cox regression model, as it accounts for the possibility of multiple potential outcomes [21]. Therefore, a Fine-Gray competitive risk model is built to compare the survival differences between patients with different characteristics. In addition, we also established a nomogram model by using R 4.3.3 data packet to present the one-year, five-year and ten-year survival rates. Finally, the prediction ability of the model is proved by C-index and calibration curve.

3. Results

3.1 Basic Characteristics of Patients Before and After PSM

From 2000 to 2021, a total of 59,873 cases of laryngeal cancer were reported in SEER database. Demographic and clinicopathological features are shown in Table 1. Table 1 summarizes the basic information and clinicopathological features of the patients. Among the 12,283 eligible patients with laryngeal cancer, 10,127 were diagnosed at the age of 50-79, accounting for 82.45% of the total number, and most of them were men, accounting for 79.23% of the total number, about four times that of women and most of them were white (80.35%). With regard to the marital status of the patients, it is clear that the majority of the patients are married. The tumor were mainly located in the glottis and the glottis, and the average size was 25 mm. In the T-class classification, the distribution of patients in each stage is relatively uniform. In the N-class classification, 7445(60.61%) patients are concentrated in the N0 stage, 2947(23.96%) patients are concentrated in the N2 stage, and patients in other stages are rare. In M-class classification, the vast majority of patients (95.55%) are concentrated in M0 stage. Of all the patients, only 221 cases (1.8%) had tumor metastasis. In the choice of treatment methods, more than half of the patients received surgery, 71.5% of patients received radiotherapy, and only 39.2% received chemotherapy. Compared with the non-operation group, there were differences in sex, tumor site, T/N/M staging, metastasis, radiotherapy and chemotherapy (SMD>0.1). Men are more likely to undergo surgical treatment compared to women. Patients with glottic tumors are also more inclined toward surgical treatment (43.52% vs. 30.56%), whereas those with supraglottic tumors are more inclined toward non-surgical treatment (38.21% vs. 58.03%). Patients in T2 and T3 stage tend to opt for non-surgical treatments, while T1 and T4 stage patients with LC are more likely to receive surgical treatment. Stage N0 patients (no regional lymph node involvement) are more often treated with surgery (64.44% vs. 56.38%), while those with lymph node involvement tend to receive non-surgical treatment, same for patients in stage M0 (no distant metastasis)., But patients with metastasis tend to opt for non-surgical options. Additionally, patients receiving radiotherapy or chemotherapy are rarely treated with surgery.

Following propensity score matching (PSM), 7,392 patients were successfully matched, and the baseline characteristics between the two groups were well-balanced, with a standardized mean difference (SMD) of less than 0.1 (Table 2).

Table 1. Baseline characteristics of patients before PSM

Variables	Overall	Nonsurgery	Surgery	P value	SMD
	n=12283	n=5837	n=6446		
Age					
<50	988 (8.04)	405 (6.94)	583 (9.04)	<0.0001	0.0877
50-79	10127 (82.45)	4834 (82.82)	5293 (82.11)		
>80	1168 (9.51)	598 (10.24)	570 (8.84)		
Race					
White	9869 (80.35)	4684 (80.25)	5185 (80.44)		
Black	1884 (15.34)	927 (15.88)	957 (14.85)	0.0271	0.0486
Other	530 (4.31)	226 (3.87)	304 (4.72)		
Gender					
Male	9732 (79.23)	4496 (77.03)	5236 (81.23)		
Female	2551 (20.77)	1341 (22.97)	1210 (18.77)	<0.0001	0.1036
Marriage					
Married	9221 (75.07)	4439 (76.05)	4782 (74.19)	0.0522	0.0439
Unmarried	2586 (21.05)	1176 (20.15)	1410 (21.87)		
Unknown	476 (3.88)	222 (3.80)	254 (3.94)		
Tumor Loction					
Glottis	4589 (37.36)	1784 (30.56)	2805 (43.52)	<0.0001	0.4221
Subglottis	319 (2.60)	108 (1.85)	211 (3.27)		
Supraglottis	5850 (47.63)	3387 (58.03)	2463 (38.21)		
Larynx, NOS	950 (7.73)	403 (6.90)	547 (8.49)		
Other	575 (4.68)	155 (2.66)	420 (6.52)		
Size	25.0 [15.0, 37.0]	25.0 [15.0, 35.0]	27.0 [15.0, 40.0]	<0.0001	0.0975
T					
T1	2905 (23.65)	1276 (21.86)	1629 (25.27)	<0.0001	0.5397
T2	2809 (22.87)	1770 (30.32)	1039 (16.12)		
T3	3146 (25.61)	1778 (30.46)	1368 (21.22)		
T4	3423 (27.87)	1013 (17.35)	2410 (37.39)		
N					
N0	7445 (60.61)	3291 (56.38)	4154 (64.44)	<0.0001	0.1734
N1	1620 (13.19)	857 (14.68)	763 (11.84)		
N2	2943 (23.96)	1523 (26.09)	1420 (22.03)		
N3	165 (1.34)	96 (1.64)	69 (1.07)		
NX	110 (0.90)	70 (1.20)	40 (0.62)		
M					
M0	11736 (95.55)	5453 (93.42)	6283 (97.47)	<0.0001	0.2018
M1	432 (3.52)	317 (5.43)	115 (1.78)		
MX	115 (0.94)	67 (1.15)	48 (0.74)		
Grade					

Grade I	1559 (12.69)	727 (12.46)	832 (12.91)	0.6881	0.022
Grade II	7229 (58.85)	3464 (59.35)	3765 (58.41)		
Grade III	3357 (27.33)	1584 (27.14)	1773 (27.51)		
Grade IV	138 (1.12)	62 (1.06)	76 (1.18)		
Metastasis					
No/Unknown	12062 (98.20)	5656 (96.90)	6406 (99.38)	<0.0001	0.1843
Yes	221 (1.80)	181 (3.10)	40 (0.62)		
Radiation					
No	3501 (28.50)	987 (16.91)	2514 (39.00)	<0.0001	0.5079
Yes	8782 (71.50)	4850 (83.09)	3932 (61.00)		
Chemotherapy					
No	7468 (60.80)	2732 (46.80)	4736 (73.47)	<0.0001	0.566
Yes	4815 (39.20)	3105 (53.20)	1710 (26.53)		

Note: T: tumor stage; N: nearby lymph node stage; M: distant metastasis stage; PSM: propensity score matching; SMD: standardized mean difference

Table 2. Baseline characteristics of patients after PSM

		PSM data set			
Variables	**Overall**	**Nonsurgery**	**Surgery**	**P value**	**SMD**
	7392	n=3696	n=3696		
Age					
<50 years	587 (7.94)	288 (7.79)	299 (8.09)	0.8155	0.0149
50-79 years	6027 (81.53)	3024 (81.82)	3003 (81.25)		
>80 years	778 (10.52)	384 (10.39)	394 (10.66)		
Race					
White	5895 (79.75)	2958 (80.03)	2937 (79.46)		
Black	1164 (15.75)	572 (15.48)	592 (16.02)	0.81	0.0151
Other	333 (4.50)	166 (4.49)	167 (4.52)		
Gender					
Female	1537 (20.79)	756 (20.45)	781 (21.13)	0.4915	0.0167
Male	5855 (79.21)	2940 (79.55)	2915 (78.87)		
Marriage					
Married	5534 (74.86)	2778 (75.16)	2756 (74.57)	0.2584	0.0383
Unmarried	1556 (21.05)	781 (21.13)	775 (20.97)		
Unknown	302 (4.09)	137 (3.71)	165 (4.46)		
Tumor Location					
Glottis	2783 (37.65)	1429 (38.66)	1354 (36.63)	0.3348	0.0497
Subglottis	186 (2.52)	89 (2.41)	97 (2.62)		
Supraglottis	3540 (47.89)	1757 (47.54)	1783 (48.24)		
Larynx, NOS	593 (8.02)	285 (7.71)	308 (8.33)		
Other	290 (3.92)	136 (3.68)	154 (4.17)		
Size	25.0 [15.0, 36.0]	25.0 [15.0, 36.0]	26.0 [15.0, 36.0]	0.0025	0.0422
T					
T1	1852 (25.05)	968 (26.19)	884 (23.92)	0.0772	0.0609
T2	1736 (23.48)	868 (23.48)	868 (23.48)		
T3	1921 (25.99)	956 (25.87)	965 (26.11)		
T4	1883 (25.47)	904 (24.46)	979 (26.49)		
N					
N0	4469 (60.46)	2257 (61.07)	2212 (59.85)	0.8576	0.0268
N1	986 (13.34)	485 (13.12)	501 (13.56)		
N2	1776 (24.03)	877 (23.73)	899 (24.32)		
N3	95 (1.29)	46 (1.24)	49 (1.33)		
NX	66 (0.89)	31 (0.84)	35 (0.95)		
M					
M0	7098 (96.02)	3544 (95.89)	3554 (96.16)	0.816	0.0148
M1	213 (2.88)	111 (3.00)	102 (2.76)		
MX	81 (1.10)	41 (1.11)	40 (1.08)		
Grade					
Grade I	979 (13.24)	493 (13.34)	486 (13.15)	0.6424	0.0301
Grade II	4343 (58.75)	2192 (59.31)	2151 (58.20)		
Grade III	1989 (26.91)	973 (26.33)	1016 (27.49)		
Grade IV	81 (1.10)	38 (1.03)	43 (1.16)		
Metastasis					
No/Unknown	7308 (98.86)	3651 (98.78)	3657 (98.94)	0.5832	0.0153
Yes	84 (1.14)	45 (1.22)	39 (1.06)		
Radiation					
No	1699 (22.98)	874 (23.65)	825 (22.32)	0.1845	0.0315
Yes	5693 (77.02)	2822 (76.35)	2871 (77.68)		
Chemotherapy					
No	4527 (61.24)	2264 (61.26)	2263 (61.23)	1	0.0006
Yes	2865 (38.76)	1432 (38.74)	1433 (38.77)		

Note: T:tumor stage; N: nearby lymph node stage; M: distant metastasis stage; PSM: propensity score matching; SMD: standardized mean difference

3.2 Analysis of Overall Survival (OS) and Laryngeal Cancer-Specific Survival (LCSS) between Surgical Group and Non-Surgical Group.

We used K-M survival curve to analyze the OS and LCSS of the surgical group and the non-surgical group. The results showed that the patients who underwent surgery had a good prognosis before and after matching, with a P value of < 0.0001 (Figure 2).

In the established competitive risk model, the cumulative mortality of patients without surgery is much higher than that of surgical patients (Figure 3A), and the specific mortality of laryngeal cancer of patients without metastatic resection is also higher than patients with metastatic resection (Figure 3B).

In multivariate cox regression analysis of PSM data set, the risk of surgical treatment on OS (HR=0.641, 95%CI 0.606 to 0.677) and LCSS(HR=0.0.585, 95%CI 0.533 to 0.641) decreased by 35.9% and 41.5% respectively (Figure 4).

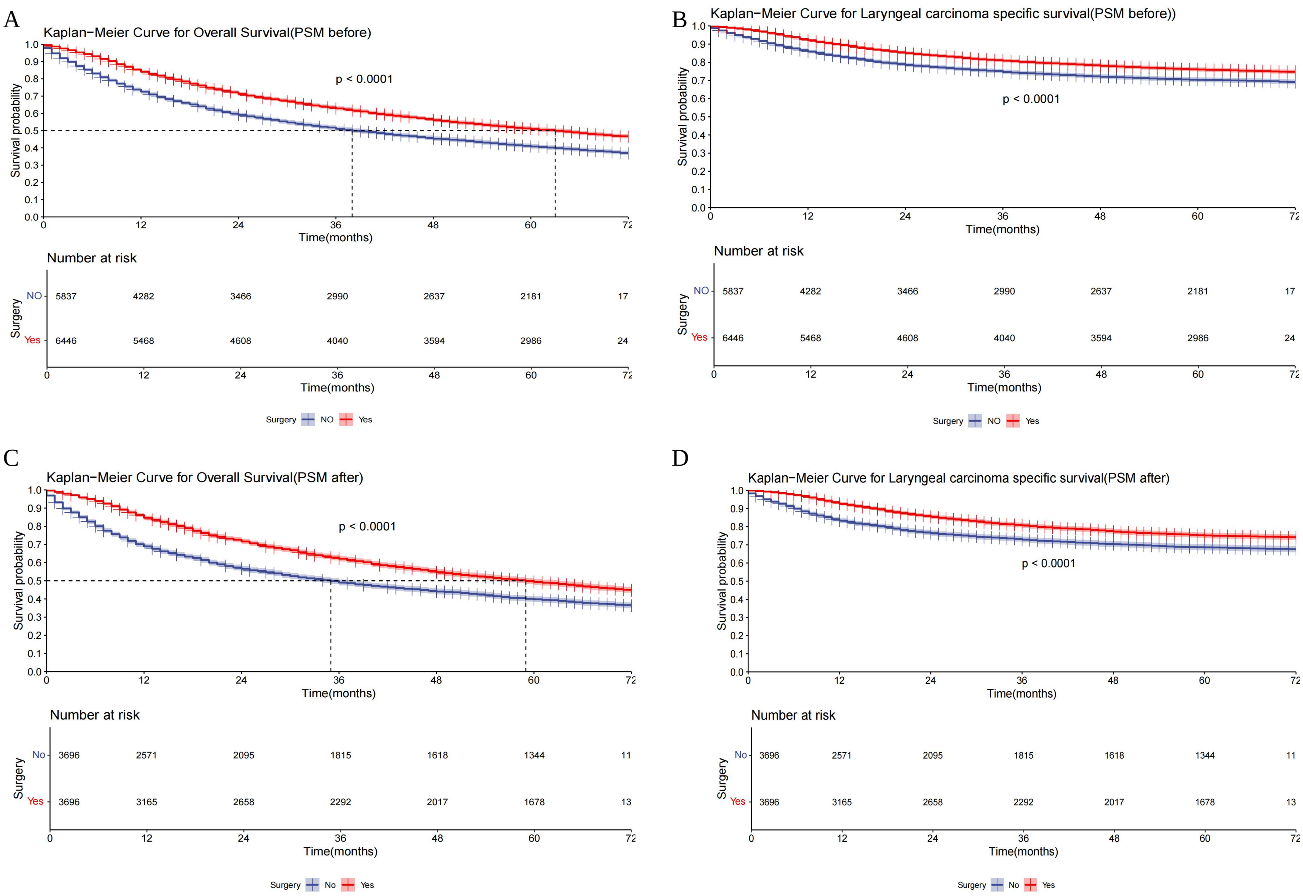

Figure 2. Kaplan-Meier curves of overall survival rate (Figure A,C) and laryngeal cancer-specific survival rate (Figure B,D) before and after propensity score matching (PSM). The figure shows the number of patients at risk at different time points and the p value of log-rank test.

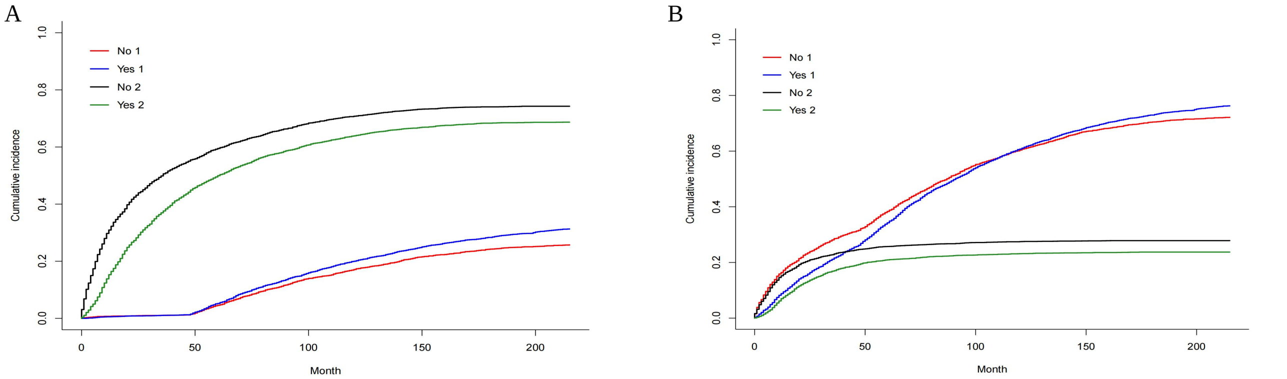

Figure 3. Competitive risk curve of cancer-specific survival between surgical patients and non-surgical patients with laryngeal cancer. (Yes represents the patient undergoing surgery, No represents surgical patient; 1 represents survival, 2 represents all-cause or specific death). A:OS competitive risk curve; (B): LCSS competitive risk curve

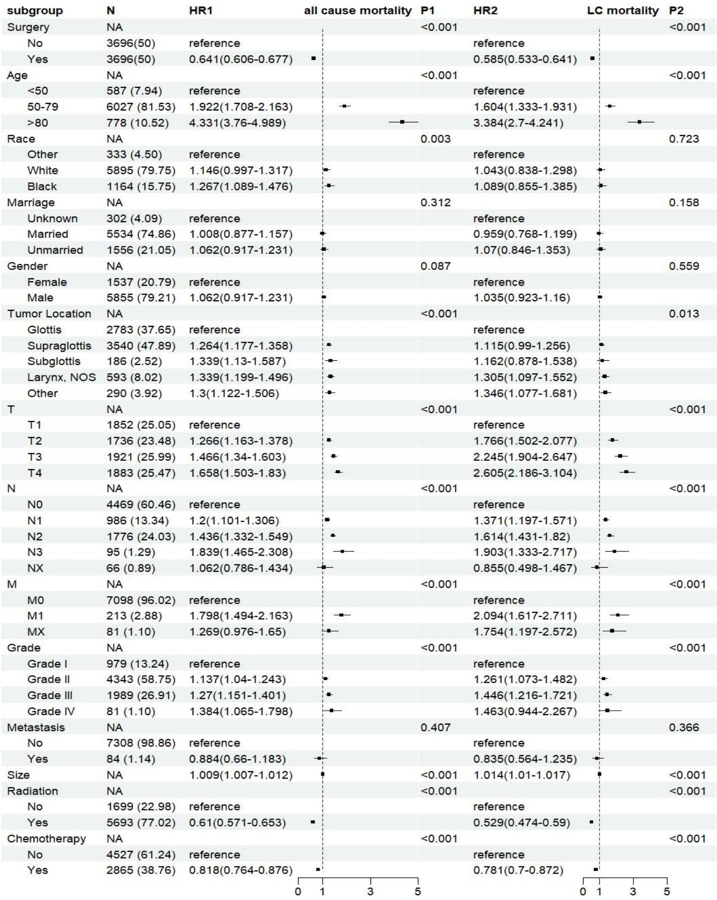

Figure 4. OR at OS and LCSS levels in patients with surgically and nonsurgically treated laryngeal cancer. OR:odds ratio; OS:overall survival; LCSS:laryngeal cancer-specific survival

3.3 Construction of Prognosis Model (Nomogram Model) for Patients Undergoing Laryngeal Cancer Surgery.

As the results of multivariate Cox regression shows, we chose meaningful variables (P<0.05) to construct the OS and LCSS prognosis models of laryngeal cancer patients, and the influencing factors included were age, tumor site, T/N/M stage, grade, tumor size, radiotherapy and chemotherapy. Each factor has its own corresponding score with the total score of 280. According to the corresponding scores, we can easily aquire the survival rate of one-year survival rate, five-year survival rate and ten-year survival rate. The lower the score, the higher the survival rate. The results showed that the younger the patient, the smaller the tumor, the lower the T/N/M stage and grade, and the higher the OS and LCSS of the surgical patients, the glottic tumors are more likely to benefit from the operation. In addition, surgical patients can get a better prognosis by combining radiotherapy, while combining chemotherapy can not only promote the prognosis of patients but may even have the opposite effect (Figure 5).

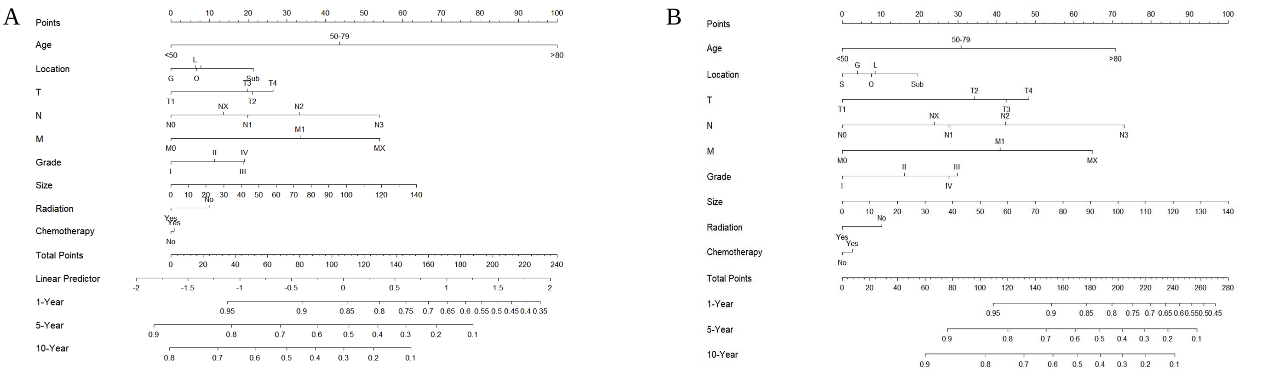

Figure 5. Nomogram model of patients undergoing laryngeal cancer surgery. (A): OS; (B): LCSS (the location variable S: supraglottic; G: glottic; O: other; L: laryngeal; Sub: subglottic)

3.4 Verification of Validity of Nomogram Prediction Model

According to the established training set and verification set, the built model is verified internally. The results show that the nomogram model of OS and LCSS prognosis of laryngeal cancer patients has high prediction accuracy. The C-index of nomogram model of patients' OS in training set and verification set is higher than TNM staging evaluation system, and the C-index of the nomogram model of patients with LCSS in training set and verification set is also improved compared with TNM staging evaluation system (Table 3).

At the same time, in order to reduce the over-fitting phenomenon of the C-index, the calibration curves of patients at 1 year, 5 years and 10 years were constructed by correcting the C-index. The results showed that the 1-year, 5-year and 10-year survival prediction curves of OS and LCSS of the nomogram prediction model were in high agreement with the diagonal, suggesting that the actual observation and the predicted 1-year survival probability were in good agreement with indicated the good accuracy of constructed model (Figure 6).

Table 3. Comparison of C-index between nomogram evaluation model and T/N/M evaluation model

items	train_data	test_data
	Concordance	Concordance
OS		
nomo-graph	0.658(0.648-0.668)	0.664(0.648-0.680)
AJCC-TNM	0.619(0.609-0.629)	0.621(0.605-0.637)
LCSS		
nomo-graph	0.709(0.93-0.725)	0.741(0.719-0.763)
AJCC-TNM	0.682(0.666-0.698)	0.714(0.717-0.765)

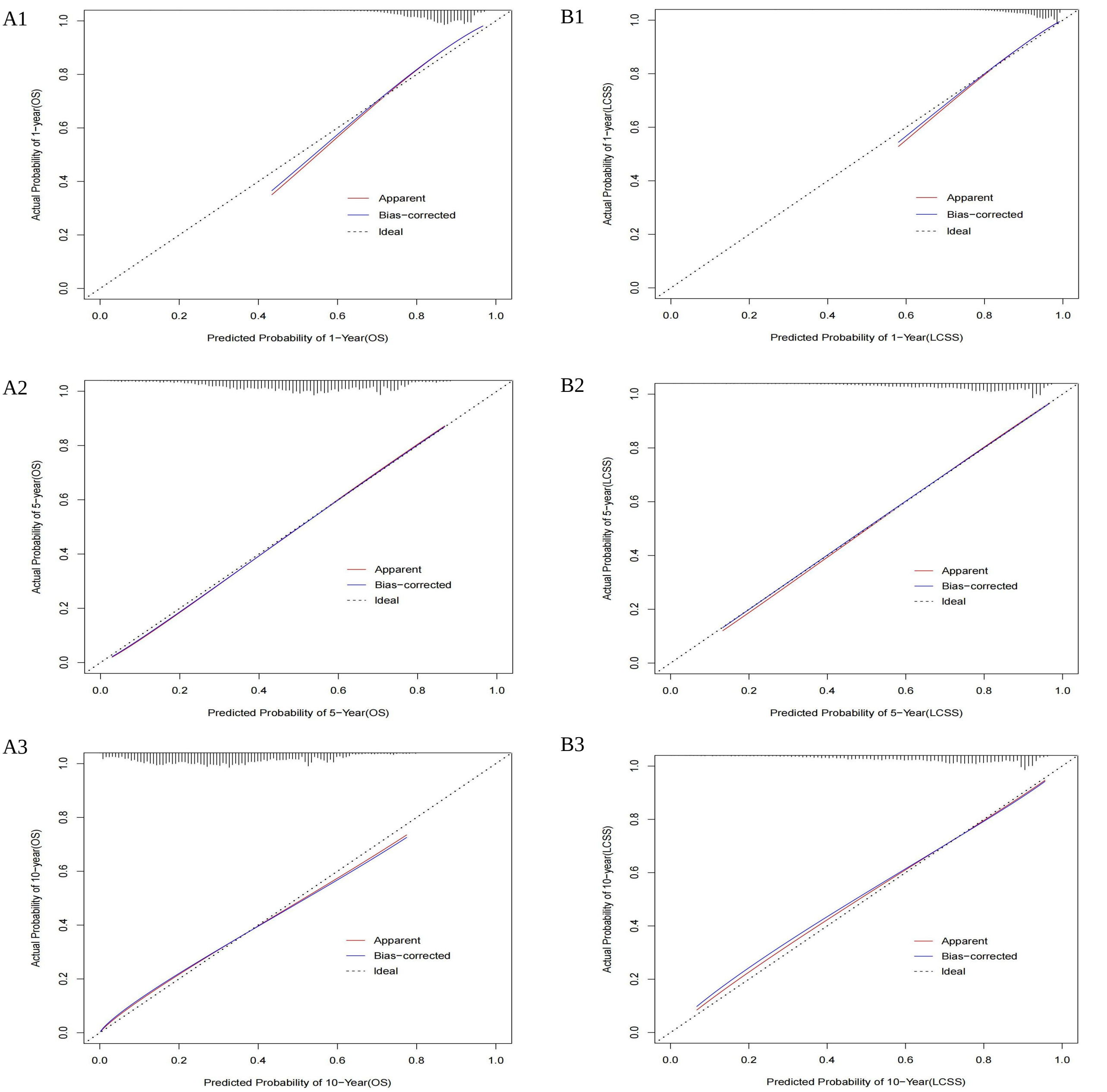

Figure 6. Calibration curves of 1-year, 5-year and 10-year survival rates of nomogram prediction models of OS (A1-A3) and LCSS(B1-B3) in patients undergoing laryngeal cancer surgery in training set and verification set (in the figure, the abscissa represents the predicted survival rate of nomogram model, the ordinate represents the actual survival rate calculated by Kaplan-Meier method, and the diagonal represents the complete matching consistency between them)

4. Discussion

This study explored the curative effect of surgery on the prognosis of laryngeal cancer patients on the basis of SEER database through retrospective cohort analysis. By including 12,283 patients. we found that laryngeal cancer patients can benefit from surgery in terms of OS rate and LCSS rate ($P<0.001$), which was consistent with many other research results. Patients with laryngeal cancer who received surgical treatment and those who received non-surgical treatment showed significant statistical differences in survival rates.

Compared to cases treated only by non-surgical methods, the prognosis of cases treated by primary surgery is obviously superior. In the clinical practice, primary surgery occupies a key position in the management of advanced LC patients [3]. In a study of spindle cell carcinoma in 2006, it was shown that the most reasonable treatment for laryngeal cancer is surgery, on the contrary, the sensitivity of radiotherapy and chemotherapy for laryngeal cancer is very low [22]. Another study also regarded high histological grade, advanced disease and no surgery as the bad factors prognosis of laryngeal neuroendocrine carcinoma. In a population-based study, surgery seems to provide a better prognosis for laryngeal verrucous cancer than other treatments [23]. The treatment of early LC (T1 and T2 lesions) hinges on the tumor location and infiltration and its spread to surrounding structures. More typical surgical treatments for early laryngeal cancer include endoscopic oral laser resection, endoscopic oral robot resection and open resection. However, it was reported that chemotherapy and immunotherapy are both not suitable for early LC [24]. In order to reduce toxic reactions, some scholars believe that early laryngeal cancer should be treated with a single treatment method as much as possible [25]. For advanced laryngeal cancer, patients who undergo total laryngectomy have a longer survival period than those who receive laryngeal preservation therapy (radiotherapy, chemotherapy, etc.), and it is the main treatment method for advanced laryngeal cancer [26]. However, due to patients' pursuit of quality of life, many late stage laryngeal cancer patients still choose to preserve their larynx, but the prognosis is poor [27].

This study demonstrates that the combination of chemotherapy and surgery has limited therapeutic benefit for patients with laryngeal cancer. Rather than improving prognosis, this combination may have adverse effects, potentially negatively impacting the outcomes of patients undergoing surgery. However, some of the past research have shown inductive chemotherapy (IC) plays a key role in organ preservation scheme in the therapeutic schedule of advanced LC patients. Those patients who are not sensitive to chemotherapy can preserve more organs and minimize the risk of surgery [28]. Some combination therapies including chemotherapy and induction therapy have shown promising prospects in laryngeal cancer. The results of a study from the Department of Veterans Affairs indicate that the combination of chemotherapy and radiation therapy is more cost-effective than the combination of surgery and radiation therapy [27]. Non-surgical methods combining chemotherapy and radiotherapy have been built up as the curing standard for advanced LC patients, because it can preserve the larynx and achieve meaningful long-term survival in some patients [29]. It was proved that IC followed by radiotherapy could preserve the larynx of most LC patients without affecting their survival rate. The treatment of LC is gradually developing. Currently, commonly used treatment schemes include conservative surgery, concurrent radiotherapy and chemotherapy, RT after IC and alternate radiotherapy and so on. IC is considered as a milestone of non-surgical laryngeal preservation [30]. This difference may be related to the type of tumor, the stage of tumor, the order of surgery and chemotherapy, etc. Chemotherapy and radiotherapy play an important role in laryngeal preservation treatment. Chemotherapy and radiotherapy play an important role in laryngeal preservation treatment. Although induction chemotherapy and synchronous chemotherapy regimens mainly based on cisplatin have been proven to play an important role in locally advanced laryngeal cancer, there is still a lack of evidence to prove that chemotherapy is superior to surgery. Further research is needed on the effects of chemotherapy on different laryngeal cancer patients and its combined application with different treatment methods [6].

Besides, we also observed that the combined application of radiotherapy and surgery showed a good therapeutic effect. Adjuvant radiotherapy after total laryngectomy is the main treatment method for advanced malignant tumors [27], when stratified by stages, the survival rate of patients with AJCC stage IV diseases in combined surgery and radiotherapy is significantly high [31]. However,According to reports, radiotherapy alone has a higher control rate for early glottic tumors, but for slightly advanced tumor cases, surgery is a better option [32,33]. Therefore, in general, radiotherapy alone is only suitable for some small early-stage tumors. Although there were various RT techniques to reduce adverse reactions, it still causes many adverse consequences for patients, such as difficulty swallowing, tissue necrosis, etc [34]. However, the progress of modern technology in the past three decades has greatly changed the treatment methods and reduced the side effects. Radiotherapy increasingly emphasizes precise targeted therapy, and modulated radiotherapy distributes different doses according to the risk of disease, and best avoids affecting adjacent normal tissues [25]. However, different populations have varying sensitivities to radiotherapy, which may be related to increased expression of telomere related proteins and pathways such as has-miR-138-2-3p. In response to this radiation resistance, in the future we can consider conducting radiation resistance testing and developing personalized treatment plans based on different patients [35,36]

In addition to treatment methods, many other factors also significantly affect the survival rate and prognosis of laryngeal cancer patients, and even affect their sensitivity to treatment. The multivariate Cox regression results showed that glottic tumors more easily benefit from surgery, especially since early glottic cancer responds quite well to surgical intervention because of its early presentation and the low incidence of local and distant metastases [37]. The results of a recent study showed that quitting smoking significantly increased treatment efficacy, survival without laryngectomy, and overall survival in laryngeal cancer patients with a history of smoking [38]. For that, Therefore, quitting smoking should become one of the first-line treatment options for laryngeal cancer. Age is an important prognostic factor for laryngeal cancer as well [14]. The nomogram shows that patients under 50 years old have the highest prognosis OS and LCSS. At the same time, the lighter the degree of T/N/M staging and grading, the better the prognosis, suggesting that early surgery can bring better therapeutic effect. Compared to younger patients, the overall perioperative survival of elderly patients is poorer. LOS and 30 day readmission can lead to a higher risk of mortality [39]. For the elderly patients, the further studies should look for more effective treatment. Compared to T/N/M staging, the construction of nomogram can better predict the survival time of LC patients undergoing surgery and offer more information for the selection of clinical therapy methods.

Research indicates that patients diagnosed with laryngeal cancer take into account not only the efficacy of treatments and survival probabilities, but also give equal weight to the functionality of organs, including their ability to swallow and speak [40]. Therefore, with the advances in medical technology,and the expanded range of treatment options for LC patients, we are supposed to emphasized the importance of conservative functional preservation surgery treatment [41]. Due to the complexity of the disease and the diversity of patients, Clinicians need to strictly evaluate the patient's condition and related indicators to determine those patients who tend to benefit from surgery. When evaluating surgical approaches for laryngeal cancer, several factors must be taken into account, such as the extent of the disease, visualization of the tumor, accessibility, and the patient's medical comorbidities. Additional important considerations include both objective and subjective factors, such as the patient's baseline vocal function, pre-treatment swallowing impairments, and logistical aspects related to the treatment process [42].

The advantages of this study are as follows: 1. The data of this study sources from the latest seer database, and the OS and LCSS rate were evaluated based on the clinical data collected in the real world, which improves the authenticity and timeliness of the study and further verifies the effect of surgery on prognosis of LC patients; 2. In this study, the PSM was used, and the interference of confounding factors was strictly controlled, and a Fine-Gray competitive risk model was constructed, and the results were more real and reliable. 3. This study focuses on key clinical demographic and pathological characteristics, which makes our study more applicable to clinical practice. A comprehensive analysis was conducted to evaluate the sensitivity of different subgroups to surgical treatment, helping to identify LC patients subgroups that are most likely to benefit from surgery. Additionally, the nomogram prediction model provides a more accurate assessment of patient prognosis, offering valuable evidence to guide individualized treatment strategies in clinical practice ; 4. We are not limited to the single treatment method of surgery, but also analyze the combined application effect of surgery, radiotherapy, chemotherapy and other common treatment methods, so as to provide more options for clinical patient selection.

Limitations of this study: 1. seer database, the data source of this study, only collects the information of patients in the US, and the results are difficult to be extended to the world. At the same time, many pathological features and treatment information such as family history of LC, complications, immunotherapy and individual chemotherapy schemes are not available; 2. The scope of this study is large, involving the whole laryngeal tumor, so the results may not be accurate to the specific subtype of LC, so it needs to be confirmed by further research.

5. Conclusion

Surgery can reduce the risk of OS and LCSS of LC patients by 35.9% and 41.5% respectively. Patients with younger age and less tumor degree can benefit more from the operation. The combined application of surgery and radiotherapy can improve the prognosis of patients, but the advantages of combined application with chemotherapy are not obvious. Compared to T/N/M staging, the constructed nomogram can better predict the outcome of patients undergoing LC surgery.

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