Prognostic factors of patients with initially diagnosed T1a glottic cancer
Novel nomograms and a propensity-score matched cohort analysis

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Abstract
The option of T1a glottic cancer treatments remarkably varied in different countries. This study aimed to construct predictive models to predict overall survival (OS) and cancer-specific survival (CSS) of patients with initially diagnosed T1a glottic cancer. And we used propensity score matching (PSM) to reassess the effect of treatments.

Data of patients with initially diagnosed T1a glottic cancer were extracted from the Surveillance, Epidemiology, and End Results database. Patients with complete information were randomly divided into the training and the validation cohorts (7:3). Cox regression was conducted to screen significant predictors of the OS and the CSS. PSM was performed to mimic randomized controlled trials. Survival analyses were performed by Kaplan–Meier survival methods, and log-rank tests were utilized.

A total of 2342 patients met the inclusion criteria. Survival analyses showed that patients who underwent primary site surgery would have better OS and CSS. Univariate analyses and multivariate analyses proved that stage, N stage, primary site surgery, and chemotherapy significantly affected both the OS and the CSS. Predictive nomograms were established to predict patients' prognosis. Finally, the OS and the CSS for patients who underwent primary site surgery alone were significantly longer than those who underwent radiation alone before and after PSM.

We constructed nomograms predicting the OS and the CSS of patients with initially diagnosed T1a glottic cancer. Compared to our previous studies, this study indicated that primary site surgery may be superior to radiation and chemotherapy. At present, chemotherapy should be not recommended for T1a glottic cancer patients.

Abbreviations: AJCC = American Joint Committee on Cancer, CI = confidence interval, CSS = cancer-specific survival, HR = hazard ratio, OS = overall survival, PSM = propensity score matching, SEER = The Surveillance, Epidemiology, and End Results.

Keywords: glottis, neoplasms, nomograms, SEER program, survival

1. Introduction
Laryngeal cancer is one of the most common types in the malignancies of head and neck\textsuperscript{[1–3]} which often occurs in the glottis\textsuperscript{[4,5]} because lymph node metastasis was rare, especially in T1a glottic cancer, patients' prognosis was often satisfactory\textsuperscript{[6,7]}. However, there is still a fierce controversy that the option of T1a glottic cancer treatments varied remarkably in different countries because of its relative rarity.

To date, frequently-used treatment options for T1a glottic cancer are primary site surgery and radiation. These 2 methods have their special advantages and disadvantages, and many published studies proved that there is still no consensus on the specific indication\textsuperscript{[8–10]}. Our previous study proved that no statistical difference was identified between surgery and radiation groups in terms of local control, overall survival (OS), and cancer-specific survival (CSS). And T1a glottic cancer patients who underwent surgery may benefit from increased larynx preservation rate compared with radiation\textsuperscript{[11]}. Over the past years, some studies indicated the positive role of chemotherapy in the treatment of advanced laryngeal cancer patients\textsuperscript{[12–14]}. Nevertheless, an obvious limitation was that previous studies of T1a glottic cancer were mainly conducted based on small, single-institutional patient cohorts, strongly influencing the reliability of their conclusions. Currently, it is noteworthy that the choice of therapeutic strategy is still left to the discretion of
doctors (surgeon or radiotherapist) and patients. Thus, the effect of various treatments in T1a glottic cancer patients remains contentious and a multicenter study with a larger sample size would be eagerly needed.\textsuperscript{15,16}

The Surveillance, Epidemiology, and End Results (SEER) database, covers about 34.6\% of the US population, which provides data of cancer incidence, patient demographics, primary tumor site, stage at diagnosis, treatments, and survival.\textsuperscript{16,17} Data collection continues to expand with a large multicenter sample. Thus, we utilized the SEER database to screen the prognostic factors and determine the optimal treatment for T1a glottic cancer patients. In our study, we concentrated on prognostic factors of age, sex, race, marital status, Grade, stage, N stage, M stage, and treatments on the OS and the CSS.

Nomography, a visual and convenient tool to quantify risk by significant clinical factors, has been widely applied to predict survival rates of individual patients.\textsuperscript{18,19} Nomogram has shown good accuracy, which could be helpful in clinical decision making, individual treatment, and clinical trial design.\textsuperscript{20} Therefore, after performing Cox hazards regression analyses to screen significant prognostic factors affecting the OS and the CSS of T1a glottic cancer, we developed nomograms to predict the prognosis for T1a glottic cancer patients. Propensity score matching (PSM), an optimal matching algorithm, can help us reduce selection bias in retrospective studies and strengthen the credibility of our research.\textsuperscript{21,22} Imbalanced distributions of the confounding factors and selection bias always existed in a retrospective observational study or the research based on national cancer registries, which may result in flawed outcomes.\textsuperscript{21,23} PSM was performed to mimic randomized controlled trials and reduce selection bias. Therefore, we conducted PSM to create a new sample and then compare the effect of treatments.

To our knowledge, our study is the first attempt to draw prognostic nomograms for T1a glottic cancer. And it is a multicenter study with a larger sample size and large-scale. Therefore, it could assist in T1a glottic cancer patients’ counseling and guide clinical treatment decision making.

2. Materials and methods

2.1. Study population

The data of eligible patients initially diagnosed as T1a glottic cancer was extracted from the SEER database (SEER ID: 18065-Nov2018). SEER*stat software version 8.3.6 (National Cancer Institute, www.seer.cancer.gov/seerstat) was applied to grab the data from the SEER 18 registry (a population-based cancer surveillance registry from 18 geographic regions) with additional treatment from 1973 to 2016.

Patients initially diagnosed as T1a glottic cancer that have met the inclusion criteria for this study were included. For all included patients in the SEER database, tumor stages were given according to the 7th American Joint Committee on Cancer (AJCC). Variables included age, sex, race, marital status, Grade, stage (AJCC, 7th edition, 2010), N stage, M stage, primary site surgery, radiation, chemotherapy, and year of diagnosis. According to the age at diagnosis, patients were divided into 2 groups of $<65$ and $\geq65$ years old. The race contained black, white, and other (American Indian/AK Native and Asian/Pacific Islander).

The exclusion criteria:

1. not the initial tumor or the only one tumor;
2. without complete information (age, race, sex, marital status, Grade, stages, treatments, cause of death, status, and survival months)
3. stages were not accessed (for example, NX and MX).

The patient consent and ethical approval for this study were not applicable since the data of the SEER database are publicly available.

2.2. Statistical analysis

Survival analyses were performed by Kaplan–Meier survival methods, and log-rank tests were utilized to detect whether differences were statistically of significance or not. All the eligible T1a glottic cancer cases were randomly divided into either the training or the validation cohorts (the split ratio was 7:3). And the training cohort was used to establish predictive models and construct nomograms. Validation of predictive models was conducted using the validation cohort.

Cox proportional hazards regression model was conducted to calculate the hazard ratio (HR) and 95\% confidence interval (CI). Univariate Cox proportional hazards models were performed to assess each parameter’s power in predicting the OS and the CSS. Then factors with $P<.05$ in univariate analyses were further assessed in multivariate Cox proportional hazards models to determine significant prognostic factors. Afterward, variables with $P<.05$ and special variables with the clinical importance were finally included to build the nomogram. The nomogram performance was quantified by calibration curves. Calibration curves were graphically drawn to show the relationship between actual probabilities\textsuperscript{24}.

The difference of the count data was tested by the Chi-square test or Fisher exact tests. Statistical analysis was conducted using R (Version 3.6.0, R Foundation, http://www.r-project.org/). $P<.05$ (2 sides) was considered statistically of significance.

2.3. Propensity score matching (PSM)

PSM can reduce selection bias and balance distributions of confounding factors.\textsuperscript{21,23} Thus, we performed a 1:1 match for each patient. A propensity score is the conditional probability of assignment to a specific treatment given a vector of covariates, which was calculated using the “MatchIt” package of R. Matching results were created through the “nearest” matching method and a caliper of 0.05. Every case of the surgery group would be matched to the radiation group according to the closest propensity score. After PSM, Chi-squared tests or Fisher exact tests were applied to detect the statistical difference of each factor between 2 treatment groups.

3. Results

3.1. Patients characteristics

A group of 3008 patients with T1a glottic cancer were identified. The flow diagram for our study about screening and grouping is shown in Figure 1. Thus, the original data containing a total of 2342 eligible patients with initially diagnosed T1a glottic cancer were finally analyzed in the current study (Supplementary Table 1, http://links.lww.com/MD/F132).
In terms of age, the larger distribution of patients was the age of \( \geq 65 \) years old. The ratio of males to females was approximately 7.3:1; 88% and 12% were male and female, respectively. Among terms of race and marital status, white and married were the majority, with 1976 (84.37%) and 1452 (62%), respectively. As for Grade and TNM stage, 1045 (44.62%) patients were Grade II, 2294 (97.95%) patients were stage I, 2294 (97.95%) patients were N0 stage, and 2339 (99.87%) patients were M0 stage. As for treatments, 1234 (52.69%) patients underwent primary site surgery, 1605 (68.53%) patients underwent radiation, whereas only 46 (1.96%) patients underwent chemotherapy.

3.2. Survival analyses of various treatments based on the original data

Of the 2342 patients in the current study, survival analyses of various treatments were performed. OS and CSS curves were shown in Figure 2. Figure 2A, 2B showed that patients who underwent primary site surgery would have better OS \( (P < .001) \) and CSS \( (P = .002) \). However, Figure 2C, 2D showed that patients who underwent radiation may suffer worse OS \( (P = .047) \) and CSS \( (P = .104) \). Moreover, Figure 2E, 2F showed that patients who underwent chemotherapy would suffer worse OS \( (P < .001) \) and CSS \( (P < .001) \). Furthermore, Figure 2G, 2H
showed that the treatment of primary site surgery or radiation may be superior to the treatment of primary site surgery and radiation in terms of patients’ OS ($P < .001$) and CSS ($P < .001$).

3.3. Patients characteristics of the training and the validation cohorts
After removing unknown/missing data, 1634 eligible patients from 2010 to 2015 were finally identified. All eligible patients
were randomly divided into the training (1146, 70%) and the validation cohorts (488, 30%). The baseline characteristics and treatments of all patients were summarized in Table 1.

### 3.4. Univariate and multivariable analyses

Cox proportional hazards models were performed in the training cohort to detect each variable’s power in predicting the OS and the CSS (Table 2). As for OS, univariate analyses suggested that factors such as age, race, marital status, stage, N, primary site surgery, radiation, and chemotherapy were likely associated with patients’ prognosis. Then multivariable analyses indicated that factors such as age, race, marital status, stage, and chemotherapy were identified as independent predictors of OS and included in the predictive model. Primary site surgery (P=.10) and radiation (P=.16) were also included in the predictive model due to their clinical importance (Fig. 3A). Because the data of N stage was the same as the data of stage, they were considered as 1 homogenous factor in multivariate analyses and N stage was excluded from nomograms.

As for CSS, univariate analyses suggested that factors such as Grade, stage, N, primary site surgery, and chemotherapy were likely associated with patients’ prognosis. Then multivariable analyses indicated that factors such as Grade, stage, N, primary site surgery, and chemotherapy were identified as independent predictors of CSS and included in the predictive model (Fig. 3B). Radiation (P=.24) was also included in the predictive model due to its clinical importance. Because the data of N stage was the same as the data of stage, they were considered as 1 homogenous factor in multivariate analyses and N stage was excluded from nomograms.

### 3.5. Building and validating novel nomograms

Predictive models were virtually plotted in the form of nomograms, which were validated using the validation cohort. For every individual patient, lines of significant prognosis factors were drawn upward to determine points. The sum of these points would be...
Table 2  
Cox regression analyses of prognostic factors affecting T1a glottic cancer patient survival in the training cohort.

| Variable                      | Overall survival | Cancer-specific survival |
|-------------------------------|------------------|-------------------------|
|                               | Univariate analysis | Multivariate analysis | Univariate analysis | Multivariate analysis |
|                               | HR(95%CI) | P | HR(95%CI) | P | HR(95%CI) | P | HR(95%CI) | P |
| Age, years                    |            |        |            |        |            |        |            |        |
| <65                           | Reference   | .001  | Reference   | .001  | Reference   | 1       | Reference   | 1       |
| ≥65                           | 1.67 (1.23–2.28) | .001  | 1.73 (1.27–2.37) | .001  | 1.00 (0.66–1.51) | 1       | 1.00 (0.66–1.51) | 1       |
| Sex                           |            |        |            |        |            |        |            |        |
| Female                        | Reference   | .60   | Reference   | .60   | Reference   | .48     | Reference   | .48     |
| Male                          | 0.89 (0.58–1.38) | .60   | 1.30 (0.63–2.68) | .48   | 1.30 (0.63–2.68) | .48     | 1.30 (0.63–2.68) | .48     |
| Race                          |            |        |            |        |            |        |            |        |
| Black                         | Reference   | .20   | Reference   | .20   | Reference   | .64     | Reference   | .64     |
| White                         | 0.75 (0.49–1.17) | .20   | 0.83 (0.53–1.29) | .40   | 0.83 (0.53–1.29) | .40     | 0.83 (0.53–1.29) | .40     |
| Other (American Indian/AK Native, Asian/Pacific Islander) | 0.21 (0.05–0.91) | .04   | 0.27 (0.06–1.16) | .08   | 0.24 (0.03–1.90) | .18     | 0.24 (0.03–1.90) | .18     |
| Marital status                |            |        |            |        |            |        |            |        |
| Unmarried                     | Reference   | .001  | Reference   | .001  | Reference   | .06     | Reference   | .06     |
| Married                       | 0.62 (0.47–0.83) | .001  | 0.65 (0.49–0.87) | .003  | 0.68 (0.45–1.02) | .06     | 0.68 (0.45–1.02) | .06     |
| Grade                         |            |        |            |        |            |        |            |        |
| Grade I&II                    | Reference   | .33   | Reference   | .33   | Reference   | .007    | Reference   | .007    |
| Grade III&IV                  | 1.25 (1.80–1.94) | .33   | 2.15 (1.27–3.63) | .004  | 2.07 (1.22–3.51) | .007    | 2.07 (1.22–3.51) | .007    |
| Stage (AJCC, 7th edition, 2010) |            |        |            |        |            |        |            |        |
| I&II                          | Reference   | .001  | Reference   | .001  | Reference   | .001    | Reference   | .001    |
| II&IV                         | 5.19 (2.29–11.74) | <.001 | 3.47 (1.48–8.15) | .004  | 8.53 (3.45–21.12) | <.001   | 8.53 (3.45–21.12) | <.001   |
| N                             |            |        |            |        |            |        |            |        |
| N0                            | Reference   | <.001 | Reference   | <.001 | Reference   | NA^     | Reference   | NA^     |
| N1&N2                         | 5.19 (2.29–11.74) | <.001 | 5.51 (2.40–12.61) | <.001 | 8.53 (3.45–21.12) | <.001   | 8.53 (3.45–21.12) | <.001   |
| M                             |            |        |            |        |            |        |            |        |
| M0                            | Reference   | .10   | Reference   | .10   | Reference   | .24     | Reference   | .24     |
| Radiation                     |            |        |            |        |            |        |            |        |
| No                             | Reference   | .007  | Reference   | .007  | Reference   | .02     | Reference   | .02     |
| Yes                           | 0.68 (0.51–0.90) | .007  | 0.77 (0.57–1.05) | .10   | 0.61 (0.41–0.92) | .02     | 0.61 (0.41–0.92) | .02     |
| Chemotherapy                  |            |        |            |        |            |        |            |        |
| No/Unknown                    | Reference   | .007  | Reference   | .007  | Reference   | .24     | Reference   | .24     |
| Yes                           | 1.62 (1.14–2.30) | .007  | 1.31 (0.90–1.90) | .16   | 1.33 (0.83–2.15) | .24     | 1.33 (0.83–2.15) | .24     |
| Year of diagnosis             |            |        |            |        |            |        |            |        |
| 2010–2012                     | Reference   | .03   | Reference   | .03   | Reference   | .08     | Reference   | .08     |
| 2013–2015                     | 0.79 (0.56–1.13) | .20   | 0.96 (0.59–1.54) | .85   | 0.96 (0.59–1.54) | .85     | 0.96 (0.59–1.54) | .85     |

^Because the number of N stage was the same as the data of stage (AJCC, 7th edition, 2010), they were considered as one homogenous factor in multivariate analyses.

^After detecting unknown/missing data, no patients of M1 stage were finally included.

Located on the “Total Points” axis. Besides, the other lines were drawn downward to determine the possibility of 3- and 5-year OS (Fig. 4A) or CSS (Fig. 4B) for patients according to total points. Calibration curves showed good consistency between the actual observation and the nomogram prediction in the probability of 3- and 5-year OS and CSS (Fig. 5).

3.6. Patients’ characteristics of primary site surgery alone and radiation alone groups before and after PSM

Before PSM, the data of 1108 patients contained 417 patients who underwent primary site surgery alone, and 691 patients who underwent radiation alone (Table 3). Comparing the primary site surgery alone and radiation alone groups, there were statistically significant differences in patients characteristics, including marital status (P = .006), stage (P = .03), and chemotherapy (P = .02).

After PSM, 414 pairs of patients were successfully matched (Table 3). Characteristics such as age (P = .68), sex (P = .74), race (P = .99), marital status (P = .70), stage (P = 1), N (P = 1), M (P = 1), chemotherapy (P = 1), and year of diagnosis (P = .78) were all without a significant difference.

3.7. Survival analyses of primary site surgery alone vs radiation alone before and after PSM

OS and CSS curves before and after PSM were plotted in Figure 6. Before PSM, patients who underwent primary site surgery alone would have better OS (P < .001) and CSS (P = .003) than patients who underwent radiation alone (Figure 6A, 6B). After PSM, Figure 6C, 6D also proved that patients who underwent primary site surgery alone would have better OS (P < .001) and CSS (P < .001) than patients who underwent radiation alone.

4. Discussion

Glottic cancer is common and represented approximately 52.03% of laryngeal cancer in the SEER database, in which
T1a glottic cancer represents about 7.38% of laryngeal cancer. T1a glottic cancer is one of early-stage glottic cancer and often has an excellent prognosis.\[6,7,26\] However, owing to its high discrepancy in treatment options for different patients, survival rates of T1a glottic cancer still varied significantly. To date, predictive models of T1a glottic cancer for predicting the prognosis is blank. There are also no reliable guidelines for the treatment of T1a glottic cancer. Therefore, developing prognostic
models is 1 meaningful approach to predict patients' outcomes and determine better therapeutic strategies.

With survival analyses of treatments based on the original data, we found that primary site surgery would indicate better OS and CSS compared with non-surgery, whereas radiation may decrease patients' OS compared with non-radiation. And chemotherapy would lead to worse OS and CSS. Understandably, primary site surgery would improve patients' prognosis.

\[\text{CSS} = \text{cancer-specific survival}, \text{OS} = \text{overall survival}\]
Figure 5. The calibration curves for predicting patients’ prognosis. (A) 3-year OS in the training cohort. (B) 5-year OS in the training cohort. (C) 3-year CSS in the training cohort. (D) 5-year CSS in the training cohort. (E) 3-year OS in the validation cohort. (F) 5-year OS in the validation cohort. (G) 3-year CSS in the validation cohort. (H) 5-year CSS in the validation cohort. CSS = cancer-specific survival, OS = overall survival.
Surprisingly, patients who underwent radiation or chemotherapy may suffer worse patients’ prognosis. After screening literature, we found studies cannot set a blank control group (patients without primary site surgery, radiation, or chemotherapy) to assess the effect of treatments.\[27–29\]

Both primary site surgery and radiation have benefits and drawbacks. Primary site surgery is quick, inexpensive, and repeatable after the event of recurrence.\[28,30\] But it requires a foundation of solid surgical expertise and the feasibility of surgery will depend on patients anatomy. While, radiation can avoid general anesthesia and lead to a possibility of better functional outcomes, but is actually a longer treatment and may lead to adjacent tissues with some sequelae such as fibrosis, mucosal edema, and laryngeal chondronecrosis.\[27–29\] In terms of chemotherapy, a recent ten-year study also pinpointed that the curative effect of chemotherapy for LC patients remained uncertain, and the toxicity profile would possibly be significant.\[15\] Thus, chemotherapy was often recommended for advanced glottic cancer patients in some studies and practice guidelines, such as the NCCN (National Comprehensive Cancer Network) Clinical practice guideline.\[14,31,32\] And chemotherapy would likely be not suitable for T1a glottic cancer. Furthermore, patients who underwent primary site surgery or radiation would have a better OS and CSS than patients who underwent primary site surgery and radiation. It may indicate that primary site surgery alone may likely be the preferred treatment and may have no need to perform the combination therapy.

With univariate and multivariate analyses of the training cohort, we confirmed that age, marital status, stage, N, and chemotherapy are associated with patients’ OS, while Grade, stage, N, primary site surgery, and chemotherapy are associated with patients’ CSS. It also proved that primary site surgery was a independent prognostic factor, whereas chemotherapy was a vital independent prognostic factor decreasing patients OS and CSS. And then we established and validated nomograms to predict 3- and 5-year OS and CSS of T1a glottic cancer patients visually and intuitively based on these significant factors and treatments with clinical importance. The validation of models using different statistical methods demonstrated its great performance.

It is noteworthy that one of the most important risk factors impacting patients’ prognosis is chemotherapy, which is considered as a significant predictor of decreasing OS and CSS. Vokes et al indicated that the rates of acute toxic effects were higher in chemotherapy groups.\[33\] Consequently, the poor prognosis may be primarily due to the toxicity of chemotherapy. However, there are still 2 concerns regarding chemotherapy in T1a glottic cancer that remain to be solved. The most vital concern is that there is no generally accepted standard regimen of chemotherapy for T1a glottic patients. Additionally, in the current study, because the

| Variable | Before PSM | After PSM |
|----------|------------|-----------|
| | Primary site surgery alone (N=417) | Radiation alone (N=691) | P | Primary site surgery alone (N=414) | Radiation alone (N=414) | P |
| Age, years | | | .16 | | | .68 |
| <65 | 201 | 302 | | 199 | 192 | .68 |
| ≥65 | 216 | 380 | | 215 | 222 | |
| Sex | | | .80 | | | .74 |
| Female | 50 | 78 | | 47 | 43 | .74 |
| Male | 367 | 613 | | 367 | 371 | .74 |
| Race | | | .16 | | | .99 |
| Black | 33 | 76 | | 33 | 32 | .99 |
| White | 362 | 588 | | 361 | 362 | |
| Other (American Indian/AK Native, Asian/Pacific Islander) | 22 | 27 | | 20 | 20 | |
| Marital status | | | .006 | | | .70 |
| Unmarried | 126 | 267 | | 125 | 119 | .70 |
| Married | 291 | 424 | | 289 | 295 | |
| Grade | | | 1 | | | 1 |
| Grade I & II | 378 | 627 | | 376 | 376 | 1 |
| Grade III & IV | 39 | 64 | | 38 | 38 | |
| Stage (AJCC, 7th edition, 2010) | | | .03 | | | .03 |
| I & II | 417 | 683 | | 414 | 414 | .03 |
| III & IV | 0 | 8 | | 0 | 0 | .03 |
| N | | | 1 | | | 1 |
| N0 | 417 | 683 | | 414 | 414 | 1 |
| N1 & N2 | 0 | 8 | | 0 | 0 | 1 |
| M | | | 1 | | | 1 |
| MO | 417 | 691 | | 414 | 414 | 1 |
| Chemistry | | | .02 | | | .02 |
| No/Unknown | 416 | 676 | | 413 | 413 | .02 |
| Yes | 1 | 15 | | 1 | 1 | .02 |
| Year of diagnosis | | | .68 | | | .78 |
| 2010–2012 | 201 | 343 | | 200 | 205 | .78 |
| 2013–2015 | 216 | 348 | | 214 | 209 | .78 |
details of chemotherapy for patients can not be acquired from the SEER database, subgroup analyses according to specific chemotherapy regimen can not be conducted.

Another significant factor was primary site surgery. The CSS of patients who underwent primary site surgery is far better than patients without primary site surgery. Canis et al included 400 T1a glottic cancer to assess the effect of transoral laser microsurgery. Transoral laser microsurgery has advantages of a low complication rate, an excellent functional outcome, and a high rate of organ preservation. Moreover, Landolfo et al reported that transoral laser surgery showed similar oncologic outcomes compared with open cordectomy. As shown in Table 3, patients characteristics of primary site surgery alone and radiation alone groups (after deleting unknown data) were distributed unevenly, and several vital variables were proved as independent prognostic factors. Hence, PSM was applied to reduce selection bias and balance distributions of the confounding factors. After PSM, the variables distribution between primary site alone and radiation alone groups were well balanced. Figure 5 showed that patients who underwent primary site surgery alone had significantly a better OS and CSS compared with patients who underwent radiation alone before and after PSM. Low et al reported that the 5-year OS for T1a glottic cancer patients treated with surgery vs radiation was 86% vs 85%, and laryngectomy-free CSS was 100% vs 88% \( (P=0.03).^{[35]} \) Thurnher et al also proved that 5-year, 10-year, and 15-year CSS for laser-treated T1a glottic cancer patients were all 100%, for conventional surgery were 100%, 98%, and 98%, and for radiation were 96%, 92%, and 91%, respectively. Moreover, the mortality rate caused by the laryngeal tumor was significantly higher in the radiation group \( (P=0.003). \) Vaculik et al’s meta-analysis suggests that transoral laser microsurgery is superior to radiation for T1 glottic cancer in terms of the OS, the CSS, and laryngeal preservation rate. There are several limitations in our study. Our study was a retrospective study with inherent biases, although we used PSM to control the bias. Moreover, predictive models were developed based on data obtained from the SEER database, potentially limiting the generalizability of our conclusions. Thus, even though we did internal verifications, larger prospective studies are still required. Besides, due to the limitations of the SEER database, the details of the chemotherapy regimens and

![Figure 6. Survival analyses of primary site surgery alone versus radiation alone before and after PSM. (A) Patients OS before PSM. (B) Patients CSS before PSM. (C) Patients OS after PSM. (D) Patients CSS after PSM. CSS = cancer-specific survival, OS = overall survival, PSM = propensity score matching.](image-url)
radiotherapy doses could not be obtained, which hindered further prognostic analyses based on detailed treatment schemes. Finally, despite the OS and the CSS, the cost, the risk of a second location, the duration of treatment, and quality of life (including voice quality) may better be taken into account to determine the optimized choice for T1a glottic cancer.[6,37] The SEER database also lacked information about these above factors. Compared with surgery, our previous meta-analysis confirmed that patients undergoing radiation may have the advantage of increased voice quality, including the maximum phonation time and decreased fundamental frequency.[18]

5. Conclusion

We built nomograms for predicting the OS and the CSS of patients with initially diagnosed T1a glottic cancer. The current results can be useful for T1a glottic cancer patients’ counseling and guide clinical treatment decision making. Compared to our previous studies, this study indicated that primary site surgery may be superior to radiation and chemotherapy. At present, chemotherapy should be not recommended for T1a glottic cancer patients.

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