Development and validation of a nomogram for prognosis of sinonasal squamous cell carcinoma

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Background: Sinonasal squamous cell carcinoma (SNSCC) is a rare malignancy with varied outcomes. The aim of this study was to develop a nomogram for predicting survival of patients with SNSCC.

Methods: From the Surveillance, Epidemiology, and End Results database, we identified 1766 patients diagnosed with SNSCC between 2004 and 2015. Patients were randomly separated into a training set and a validation set in a 4:1 ratio. An external validation was also performed by a set of 74 SNSCC patients who had been treated in our department. We used the training set to build a nomogram based on stratified multivariable Cox proportional hazard models for predicting overall survival. The predictive accuracy and discriminative ability of the nomogram were determined by concordance index and calibration curve.

Results: Based on 1412 cases of the training cohort, our Cox regression analysis revealed that age, marital status, primary site, differentiation, T stage, N classification, M stage, and treatment modalities were associated with overall survival. A nomogram was established based on the results of multivariate analysis. The C-index values of the nomogram for predicting survival were superior to those of the tumor-node-metastasis staging system (0.745 vs 0.679 in the training cohort, 0.752 vs 0.656 in the validation set, and 0.678 vs 0.596 in the external validation set). The calibration plots demonstrated good consistency between the predicted and observed results.

Conclusion: We have developed a nomogram to accurately predict the clinical outcomes of SNSCC patients. This model was effective and can help clinicians to improve patient counseling. © 2019 The Authors. International Forum of Allergy & Rhinology published by Wiley Periodicals, Inc. on behalf of American Academy of Otolaryngic Allergy and American Rhinologic Society.

Key Words: sinonasal squamous cell carcinoma; nomogram; population-based; predictive tools; survival

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nomograms are superior to the tumor-node-metastasis (TNM) staging system in predicting patient survival.\textsuperscript{6,7} However, to the best of our knowledge, no nomogram for SNSCC has yet been developed.

The Surveillance, Epidemiology, and End Results (SEER) database collects information for a large population of US patients and can therefore provide a sufficient number of cases for building predictive models, especially for rare tumors. In this study, we identified prognostic indicators via the updated SEER database, developed a nomogram for visually predicting SNSCC survival, and validated the results both internally and externally.

Patients and methods

Patients

To extract data from the SEER database, we used the latest SEER*stat software released on March 6, 2018 (version 8.3.3; http://seer.cancer.gov/seerstat/). We used topography codes from the International Classification of Disease for Oncology, 3rd edition (ICD-O-3), corresponding to the primary site labeled codes for the nasal cavity and paranasal sinus (C30.0, C31.1, C31.2, C31.3, C31.8, and C31.9) to identify SNSCC patients and then select those diagnosed between 2004 and 2015. The results were then further filtered using histology (ICD-O-3) codes for conventional squamous cell carcinoma: 8070/3 (squamous cell carcinoma, NOS); 8071/3 (squamous cell carcinoma, keratinizing, NOS); 8072/3 (squamous cell carcinoma, large cell, nonkeratinizing); and 8073/3 (squamous cell carcinoma, small cell, nonkeratinizing). We also excluded patients for which there were no details regarding TNM stage, histologic grade, or treatment information. From the cases remaining, patients were randomly separated into the training set and the validation set in a 4:1 ratio, respectively. Patients’ characteristics were stratified by sex, age at diagnosis, race, and marital status. Tumor characteristics were stratified by histologic grade, primary site, and TNM stage. Tumor staging was reevaluated based on the staging criteria in the American Joint Committee on Cancer (AJCC), 7th edition.

To externally validate the nomogram model, we identified patients who were diagnosed with SNSCC between March 2011 and December 2016 at the Department of Radiation Oncology, Eye and ENT Hospital, Fudan University, Shanghai, China. We excluded any patients with a history of other malignancies, incomplete medical records, or who had been lost in follow-up.

Ethics approval

The SEER is a publicly available database, and we de-identified the data extracted from it. This retrospective study was approved by the institutional review committee of the Eye and ENT Hospital of Fudan University.

Statistical analysis

All statistical analyses were performed by R software (version 3.3.3; R Foundation for Statistical Computing, Vienna, Austria) and SPSS version 24.0 (IBM, Inc, Armonk, NY). Cumulative survival curves for each patient variable were constructed using the Kaplan-Meier method and the log rank test was adopted to compare the curves. Associations between categorical variables were compared using the $\chi^2$ test. A significant difference was defined as two-tailed $p < 0.05$. Uni- and multivariate Cox proportional hazard models were used to identify potential significant prognostic factors for the entire cohort. A nomogram was built based on the Cox proportional hazards regression model and was evaluated by Harrell’s concordance index (C-index). Calibration of the nomogram was performed by comparing the predicted survival with the observed survival. A calibration plot along the 45-degree line would indicate a perfect calibration model. Discrimination between the proposed nomogram and the 7th edition of AJCC staging system was evaluated by the area under the receiver operating characteristic curve. Competing risk analysis was also performed, as in our previous study.\textsuperscript{8,9}

Results

Patients’ characteristics

From the SEER database, we identified a total of 3251 SNSCC patients who had been diagnosed between 2004 and 2015, which accounted for approximately 45.5% of the malignancies of the sinonasal cavity. Of these, we excluded 694 patients for whom SNSCC was not the first primary tumor, 444 patients without classification regarding the TNM stage, and 347 patients without any differentiation grade. Ultimately, a total of 1766 patients were included in the study. Of these, 1412 patients were assigned to the training set, and 354 patients were assigned to the validation set. The flowchart of data selection is shown in Figure 1. Table 1 shows patients’ demographics and clinical characteristics. The median follow-up of the 1766 patients was 61 months. The overall 3- and 5-year survival rates for all patients were 59.2% and 50.0%, respectively. The median survival time was 59 months in the training set and 69 months in the validation set. The external validation data set from our department included 74 patients with SNSCC, for whom the demographics and clinical characteristics are listed in Table S1 in the Supplementary Material (online), and for whom the overall 3- and 5-year survival rates were 66.6% and 62.9%, respectively.

Construction of the nomogram

In the training cohort, univariate analysis results revealed that age ($p < 0.001$), race ($p < 0.001$), marital status ($p < 0.001$), primary site ($p < 0.001$), histologic grade ($p < 0.001$), T stage ($p < 0.001$), N classification ($p < 0.001$), M stage ($p < 0.001$), TNM stage ($p < 0.001$), surgery and radiotherapy ($p < 0.001$), and chemotherapy ($p < 0.001$), and radiotherapy ($p < 0.001$), race ($p < 0.001$), surgery
0.001) were associated with overall survival (OS; Table 2). Figure 2 shows the Kaplan–Meier estimates of OS by age, sex, marital status, race, primary site, histology grade, T stage, N classification, M stage, TNM stage, surgery and radiotherapy, and chemotherapy. Figure 3 shows Kaplan-Meier survival analyses of treatment modalities for SNSCC stratified by T stage. The competing risk analysis results yielded similar results (see Figure S1 online). These potential variables were further analyzed using multivariate analysis (Table 2). Here, we did not include TNM stage, as it was not independent of the T, N, and M stages. We constructed the nomogram based on the final multivariate model by use of a cutoff value of $p < 0.1$. Finally, age ($p < 0.001$), marital status ($p = 0.006$), primary site ($p < 0.001$), histologic grade ($p = 0.035$), T stage ($p < 0.001$), N classification ($p = 0.012$), M stage ($p = 0.080$), surgery and radiotherapy ($p < 0.001$), and chemotherapy ($p = 0.014$) were included in the model (Fig. 4). By using this model, we could predict the prognosis of patients of SNSCC. First, a vertical line was drawn up to the points row to obtain points for each variable. Then, the total score was calculated for all variables using the axis of risk of event. For example, a 56-year-old married patient, with a poorly differentiated squamous carcinoma originating from the maxillary sinus, was staged as T3N0M0 and underwent surgery and radiotherapy. The scores were 0 for age and married status, 3.8 for maxillary sinus, 5.05 for T3, 2.25 for grade, 0 for N and M stages, 1.8 for chemotherapy, and 0 for surgery and radiotherapy. The total points were 12.9 and the corresponding probability of 1-, 3-, and 5-year OS were 82%, 64%, and 53%, respectively.

**Validation of the nomogram**

We performed both internal and external validation of the nomogram. We graphed the calibration plots separately for the training set and validation set, and these plots exhibited good agreement between the nomogram and actual observations for 1-, 3-, and 5-year OS in the training and validation sets (Fig. 5). The C-index values of the nomogram for predicting survival were superior to those of the TNM staging system (0.745 vs 0.679 in the training SEER cohort, 0.752 vs 0.656 in the validation set, and 0.678 vs 0.596 in the external validation set). Figure S2 online shows that the area under the curve of the nomogram with predictions for 1-, 3-, and 5-year OS were higher than for the TNM staging system in training, validation, and external sets. These data indicate that the nomogram was superior to the TNM staging system in predicting clinical outcomes of patients with SNSCC. To conduct a Kaplan-Meier survival analysis, we then calculated the nomogram score of each patient and divided the training set into 6 groups, the validation set into 4 groups, and the external set into 2 groups. To compare these groups, we used the log rank test, which was $p < 0.001$ for the SEER training and validations sets, and $p = 0.02$ in the external validation cohort (see Fig. S3 online).
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**TABLE 1. Characteristics of training set and validation set from SEER database**

| Characteristics       | All patients (n = 1766) | Training set (n = 1412) | Validation set (n = 354) |
|-----------------------|-------------------------|-------------------------|--------------------------|
| **Age**               |                         |                         |                          |
| <60 years             | 678 (38.4)              | 546 (38.7)              | 132 (37.3)               |
| 60-69 years           | 466 (26.4)              | 376 (26.6)              | 90 (25.4)                |
| 70-79 years           | 385 (21.8)              | 303 (21.5)              | 82 (23.2)                |
| ≥80 years             | 237 (13.4)              | 187 (13.2)              | 50 (14.1)                |
| **Sex**               |                         |                         |                          |
| Male                  | 1174 (66.5)             | 936 (66.3)              | 238 (67.2)               |
| Female                | 592 (33.5)              | 476 (33.7)              | 116 (32.8)               |
| **Marital status**    |                         |                         |                          |
| Single                | 311 (17.6)              | 256 (18.1)              | 55 (15.5)                |
| Married               | 933 (52.8)              | 738 (52.3)              | 195 (55.1)               |
| Others\(^a\)          | 522 (29.6)              | 418 (29.6)              | 104 (29.4)               |
| **Race**              |                         |                         |                          |
| White                 | 1411 (79.9)             | 1122 (79.5)             | 289 (81.6)               |
| Black                 | 192 (10.9)              | 159 (11.3)              | 33 (9.3)                 |
| Others\(^b\)          | 163 (9.2)               | 131 (9.3)               | 32 (9.0)                 |
| **Primary site**      |                         |                         |                          |
| Nasal cavity          | 969 (54.9)              | 774 (54.8)              | 195 (55.1)               |
| Ethmoid sinus         | 111 (6.3)               | 89 (38.9)               | 22 (38.7)                |
| Maxillary sinus       | 686 (38.8)              | 549 (6.3)               | 137 (6.2)                |
| **Grade**             |                         |                         |                          |
| Well differentiated    | 308 (17.4)              | 255 (18.1)              | 53 (15.0)                |
| Moderately differentiated | 796 (45.1)         | 635 (45.0)              | 161 (45.5)               |
| Poorly differentiated  | 632 (35.8)              | 495 (35.1)              | 137 (38.7)               |
| Undifferentiated      | 30 (1.7)                | 27 (1.9)                | 3 (0.8)                  |
| **T classification**  |                         |                         |                          |
| T1                    | 562 (31.8)              | 442 (31.3)              | 120 (33.9)               |
| T2                    | 228 (12.9)              | 178 (12.6)              | 50 (14.1)                |
| T3                    | 277 (15.7)              | 220 (15.6)              | 57 (16.1)                |
| T4a                   | 423 (24.0)              | 344 (24.4)              | 79 (22.3)                |
| T4b                   | 276 (15.6)              | 228 (16.1)              | 48 (13.6)                |
| **N classification**  |                         |                         |                          |
| N0                    | 1480 (83.8)             | 1190 (84.3)             | 290 (81.9)               |
| N1                    | 109 (6.2)               | 86 (6.1)                | 23 (6.5)                 |
| N2                    | 166 (9.4)               | 128 (9.1)               | 38 (10.7)                |
| N3                    | 11 (0.6)                | 8 (0.6)                 | 3 (0.8)                  |

(Continued)
TABLE 1. Continued

| Characteristics          | All patients (n = 1766) | Training set (n = 1412) | Validation set (n = 354) |
|--------------------------|-------------------------|-------------------------|--------------------------|
| **M classification**     |                         |                         |                          |
| M0                       | 1720 (97.4)             | 1373 (97.2)             | 347 (98.0)               |
| M1                       | 46 (2.6)                | 39 (2.8)                | 7 (2.0)                  |
| **TNM stage**            |                         |                         |                          |
| I                        | 528 (29.9)              | 418 (29.6)              | 110 (31.1)               |
| II                       | 195 (11.0)              | 151 (10.7)              | 44 (12.4)                |
| III                      | 274 (15.6)              | 219 (15.5)              | 55 (15.5)                |
| IVA                      | 458 (25.9)              | 369 (26.1)              | 89 (25.1)                |
| IVB                      | 265 (15.0)              | 216 (15.3)              | 49 (13.8)                |
| IVC                      | 46 (2.6)                | 39 (2.8)                | 7 (2.0)                  |
| **Surgery and radiotherapy** |                       |                         |                          |
| Surgery alone            | 540 (30.6)              | 416 (29.5)              | 124 (35.0)               |
| Radiotherapy alone       | 345 (19.5)              | 285 (20.2)              | 60 (16.9)                |
| Surgery plus radiotherapy| 768 (43.5)              | 616 (43.6)              | 152 (42.9)               |
| Both not given           | 113 (6.4)               | 95 (6.7)                | 18 (5.1)                 |
| **Chemotherapy**         |                         |                         |                          |
| No/unknown               | 1155 (65.4)             | 919 (65.1)              | 236 (66.7)               |
| Yes                      | 611 (34.6)              | 493 (34.9)              | 118 (33.3)               |

* Data expressed as number (%).
* Divorced, widowed, and separated.
* Asian, Pacific Islander, American Indian, and Alaska native.
SEER = Surveillance, Epidemiology, and End Results (database); TNM = tumor-node-metastasis.

**Discussion**

In previous studies, researchers analyzed the incidence and tumor characteristics of sinonasal carcinoma based on the SEER database. In this study we have focused on building predictive models. As the diversity of pathologic types in sinonasal cancer has a significant impact on survival and treatment, we narrowed our study to the traditional squamous cell carcinoma. Last, we identified several independent prognostic factors in SNSCC patients and built a nomogram to effectively and visually predict their overall survival. The internal and external validations confirmed the validity of the predictive model. To our knowledge, this is the first attempt to build prognostic models for predicting the outcomes of SNSCC using data from a population-based database. The nomogram proposed in this study provides individual estimates of the probability of survival of patients diagnosed with SNSCC.

In 2002, the AJCC revised TNM staging classification for SNSCC. For the purpose of T staging, the nasoethmoidal complex was divided into 2 sites: nasal cavity and ethmoid sinuses. T4 lesions were divided into T4a (moderately advanced local disease) and T4b (very advanced local disease), which led to the stratifications of stage IV into stage IVA (moderately advanced local/regional disease), stage IVB (very advanced local/regional disease), and stage IVC (distant metastatic disease). Our studies demonstrate that the revised TNM stage serves as excellent survival factor of SNSCC, as shown in Figure 2G-J. However, we found that the survival curve of SNSCC with T3 stage was not separated from the curve of SNSCC with T4a stage (Fig. 2G; \(p = 0.711\)). We also found there was no difference in prognostication of OS between stage III and stage IVA (Fig. 2J; \(p = 0.418\)). These results indicate that the current TNM stage still needed to be improved. Tumor differentiation also proved to be an important predictive factor of the OS. Figure 2E shows that the higher the grade of differentiation, the worse the prognosis. Furthermore, the 5-year overall survival rates of patients with maxillary carcinoma and ethmoid carcinoma were 32.3% and 40.9%, respectively, both significantly worse than the 63.8% for nasal cavity carcinoma (Fig. 2F; \(p < 0.001\)). Cancers of the nasal cavity have substantially better survival rates than do those originating in the paranasal sinus, partly because tumors originating in the nasal cavity often tend to present symptoms earlier, which leads to diagnosis at a lower T stage. In addition, we found the proportions of poorly differentiated tumors in the nasal cavity to be significantly lower than those in the
**TABLE 2. Uni- and multivariate analyses of overall survival in the training cohort**

| Characteristics | Univariate analysis | Multivariate analysis |
|-----------------|---------------------|-----------------------|
|                 | HR (95% CI)         | p                     | HR (95% CI)         | p               |
| **Total**       |                     |                       |                       |                 |
| **Age**         |                     |                       |                       |                 |
| <60 years       | Reference           | <0.001                | Reference            | <0.001          |
| 60-69 years     | 1.157 (0.948-1.413) |                       | 1.331 (1.086-1.632)  |                 |
| 70-79 years     | 1.481 (1.208-1.816) |                       | 1.635 (1.322-2.022)  |                 |
| ≥80 years       | 2.470 (1.983-3.076) |                       | 2.558 (2.008-3.260)  |                 |
| **Sex**         |                     |                       |                       |                 |
| Male            | Reference           | 0.674                 | NA                    |                 |
| Female          | 1.035 (0.883-1.212) |                       |                       |                 |
| **Marital status** |                   |                       |                       |                 |
| Single          | Reference           | <0.001                | Reference            | 0.006           |
| Married         | 0.704 (0.575-0.862) |                       | 0.712 (0.577-0.878)  |                 |
| Others<sup>a</sup> | 0.997 (0.805-1.236) |                       | 0.794 (0.633-0.996)  |                 |
| **Race**        |                     |                       |                       |                 |
| White           | Reference           | <0.001                | Reference            | 0.335           |
| Black           | 1.771 (1.426-2.199) |                       | 1.153 (0.916-1.453)  |                 |
| Others<sup>b</sup> | 1.442 (1.117-1.860) |                       | 1.145 (0.881-1.488)  |                 |
| **Primary site** |                   |                       |                       |                 |
| Nasal cavity    | Reference           | <0.001                | Reference            | <0.001          |
| Ethmoid sinus   | 2.023 (1.497-2.735) |                       | 1.533 (1.107-2.123)  |                 |
| Maxillary sinus | 2.567 (1.497-2.735) |                       | 1.713 (1.415-2.073)  |                 |
| **Grade**       |                     |                       |                       |                 |
| Well differentiated | Reference         | <0.001                | Reference            | 0.035           |
| Moderately differentiated | 1.422 (1.130-1.790) |                       | 1.285 (1.014-1.628)  |                 |
| Poorly differentiated | 1.882 (1.492-2.375) |                       | 1.418 (1.108-1.814)  |                 |
| Undifferentiated | 2.299 (1.373-3.850) |                       | 1.682 (0.982-2.881)  |                 |
| **T classification** |                 |                       |                       |                 |
| T1              | Reference           | <0.001                | Reference            | <0.001          |
| T2              | 1.362 (1.013-1.832) |                       | 1.294 (0.952-1.758)  |                 |
| T3              | 2.490 (1.953-3.174) |                       | 2.059 (1.548-2.738)  |                 |
| T4a             | 2.583 (2.079-3.211) |                       | 2.160 (1.642-2.841)  |                 |
| T4b             | 3.953 (3.135-4.984) |                       | 3.024 (2.237-4.088)  |                 |
| **N classification** |                |                       |                       |                 |
| N0              | Reference           | <0.001                | Reference            | 0.012           |
| N1              | 1.726 (1.301-2.289) |                       | 1.148 (0.858-1.536)  |                 |
| N2              | 2.079 (1.646-2.643) |                       | 1.503 (1.167-1.936)  |                 |
| N3              | 1.924 (0.797-4.643) |                       | 1.612 (0.658-3.947)  |                 |

(Continued)
TABLE 2. Continued

| Characteristics          | Univariate analysis | Multivariate analysis |
|--------------------------|---------------------|-----------------------|
|                          | HR (95% CI)         | p         | HR (95% CI)         | p         |
|                          |                     |           |                     |           |
| M classification         |                     |           |                     |           |
| M0                       | Reference            | <0.001    | Reference            | 0.080     |
| M1                       | 3.012 (2.120-4.278)  |           | 1.394 (0.961-2.021)  |           |
| TNM stage                |                     |           |                     |           |
| I                        | Reference            | <0.001    | NA                   |           |
| II                       | 1.205 (0.862-1.684)  |           |                     |           |
| III                      | 2.461 (1.916-3.160)  |           |                     |           |
| IVA                      | 2.679 (2.148-3.341)  |           |                     |           |
| IVB                      | 3.957 (3.107-5.039)  |           |                     |           |
| IV C                     | 6.055 (4.119-8.900)  |           |                     |           |
| Surgery and radiotherapy |                     |           |                     |           |
| Surgery alone            | Reference            | <0.001    | Reference            | <0.001    |
| Radiotherapy alone       | 2.100 (1.695-2.600)  |           | 1.177 (0.917-1.511)  |           |
| Surgery plus radiotherapy| 1.136 (0.931-1.386)  |           | 0.687 (0.549-0.859)  |           |
| Both not given           | 4.751 (3.611-6.251)  |           | 2.856 (2.131-3.828)  |           |
| Chemotherapy             |                     |           |                     |           |
| No/unknown               | Reference            | <0.001    | Reference            | 0.014     |
| Yes                      | 1.486 (1.274-1.733)  |           | 0.779 (0.638-0.950)  |           |

*Divorced, widowed, and separated.

bAsian, Pacific Islander, American Indian, and Alaska native.

CI = confidence interval; HR = hazard ratio.

As previously described, the prognoses of patients with SNSCC with good differentiation were better than those with worse differentiation. Nasal cavity lesions are more likely to be surgically removed, which may also improve survival. When considering treatment modality, the better survival and tumor characteristics of patients with SNSCC whose tumors originated in the nasal cavity may require that we separate these patients from those whose tumors originated in the paranasal sinuses.

We found age to be a significant prognostic indicator for SNSCC. Most patients with SNSCC were diagnosed in their sixth decade or later. In this SEER cohort, 61.6% of patients diagnosed with SNSCC were >60 years old. Multivariate analysis showed that increasing age was associated with worse OS (60-69 years: hazard ratio [HR], 1.331; 95% confidence interval [CI], 1.086-1.632; 70-79 years: HR, 1.635; 95% CI, 1.322-2.022; ≥80 years: HR, 2.558; 95% CI, 2.008-3.260). Older patients had a higher risk of death than younger patients, partly because the former had more comorbidities and shorter expected longevities. Older patients also tended to receive more conservative treatment. Interestingly, we also found marital status to have an effect on the OS of patients with SNSCC. Married patients had better prognosis than unmarried patients, which is consistent with findings reported for other malignancies. Married status may indicate strong support from family members, which could include financial, physical, and psychological support. Therefore, married patients may exhibit better compliance with medical recommendations and less depression than unmarried patients. This implies to physicians that strengthening of patients’ social supports may improve prognosis in unmarried SNSCC patients.

Generally, surgery is the cornerstone of treatment of patients with SNSCC. Unfortunately, total resection is often difficult because SNSCC often invade proximal sites such as the oral cavity, cranial nerves, orbit, and skull base. Tumors that cannot be excised completely with an adequately safe surgical margin must undergo adjuvant radiotherapy. Surgery plus radiotherapy can increase the local control rate and improve prognosis, and is considered to be the standard treatment modality for SNSCC. In our study, we found that adjuvant radiotherapy significantly improved the OS when compared with surgery alone, except for T1 SNSCC patients (Fig. 3A-C). In T1 SNSCC, the OS of radiotherapy alone was lower than that of surgery alone ($p = 0.042$). For early resectable...
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FIGURE 2. Kaplan-Meier estimate of overall survival of patients by (A) age, (B) sex, (C) race, (D) marital status, (E) histologic grade, (F) primary site, (G) T stage, (H) N stage, (I) M stage, (J) TNM stage, (K) surgery and radiotherapy, and (L) chemotherapy. TNM = tumor-node-metastasis.

tumors, complete surgical resection may be preferred over radiotherapy. In recent years, the type of resection has varied from open surgery to endoscopic techniques, and radiation therapy has become more precise. Many studies have suggested that endoscopic surgery can achieve the same results as open surgery.\textsuperscript{27,28} Some researchers have indicated that intensity-modulated radiotherapy can reduce the toxicity of surrounding tissues but not improve the rate of survival.\textsuperscript{29,30} Further studies are required that focus on survival in relation to surgical and radiotherapy techniques.

The use of chemotherapy in treating squamous cell carcinomas of the paranasal sinus and nasal cavity remains controversial. Classically, the role of chemotherapy in SNSCC has been limited to palliative treatment of locally advanced or metastatic SNSCC. Some study results have demonstrated that induction chemotherapy has a role in organ preservation in SNSCC cases involving the orbit or brain.\textsuperscript{31,32} Some authors have argued that systemic therapy may improve locoregional control rates and reduce the frequency of metastasis, ultimately resulting in improved survival.\textsuperscript{33} However, few studies suggested that chemotherapy can improve survival. In our study, we found that the use of chemotherapy improved survival probability in locally advanced SNSCC (Fig. 3D; $p = 0.007$). Multivariate analyses also showed that patients who received chemotherapy had improved OS (HR, 0.779; 95% CI, 0.638-0.950). However, the SEER database provides no details regarding chemotherapy regimen, so the potential survival benefits of systemic therapy remain to be confirmed.

The results of our study show that multimodality therapy significantly improved the prognosis of SNSCC.
However, we cannot recommend multimodality therapy for each SNSCC patient on the nomogram. Tumor stage and the patient’s specific conditions should be considered. Based on our study, adjuvant radiotherapy should be recommended in T2-T4 SNSCC. The treatment of advanced SNSCC should also include chemotherapy. Although in our analysis we used a large cohort of patients with SNSCC, our study has several limitations. Due to the rarity of the condition, there were no T stages for frontal sinus and sphenoid sinus squamous carcinomas, so this could not be predicted using this model. Recent studies have found that positive human papillomavirus (HPV) may...
FIGURE 5. The calibration curve for predicting OS of patients at 1 year (A) 3 years (B), and 5 years (C) in the training data set (left), and at 1 year (D) 3 years (E), and 5 years (F) in the validation data set (right). The nomogram-predicted probability of OS is plotted on the x axis, and the actual OS is plotted on the y axis. OS = overall survival.
be an important prognostic factor for SNSCC. However, the HPV status of SNSCC patients included in the SEER database were all blank. Thus, we could not include HPV status in our analysis. Last, we excluded from our study some patients who lacked detailed tumor characteristics information, which may have resulted in a bias. However, we validated the prognostic models both internally and externally, which indicates that the nomogram was effective.

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Conclusion

In conclusion, based on the SEER database, we have developed and validated a nomogram that exhibited better prognostic discrimination and predictive accuracy for SNSCC. The variables included in the nomogram are routinely available. Thus, it can be readily used in clinical practice. This nomogram could be used by physicians to predict individual survival and improve patient counseling.

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