

# Survival Rates of Sinonasal Squamous Cell Carcinoma With the New AJCC Staging System

Chul Hee Lee, MD; Dong Gu Hur, MD; Hwan-Jung Roh, MD; Ki-Sang Rha, MD; Hong-Ryul Jin, MD; Chae-Seo Rhee, MD; Yang-Gi Min, MD

**Objective:** To investigate the validity of the sixth edition of the American Joint Committee on Cancer (AJCC) staging system for sinonasal squamous cell carcinoma.

**Design:** A 15-year retrospective case series review.

**Setting:** Multicenter study from tertiary care facilities.

**Patients:** Data from 113 patients diagnosed as having and treated for sinonasal squamous cell carcinoma from September 1988 through August 2003 were retrieved. Ninety patients followed up for at least 12 months were included in the study.

**Main Outcome Measures:** The TNM staging system and survival rates were analyzed using the Kaplan-Meier method to determine the mean, disease-free, and 5-year survival statistics. The effect of tumor stage on overall survival was assessed with stages defined by the fifth and sixth editions of the AJCC staging systems.

**Results:** The overall 5-year survival rate was 59.5%. Ac-

ording to the sixth edition, the survival rates of patients with stages III, IVA, and IVB tumors showed a significant difference ( $P = .002$ ). In 32 cases, the stages were changed in accordance with the criteria in the sixth edition. The group in which the stage changed from III (fifth edition) to IVA (sixth edition) showed a worse survival rate than the group in which the stage did not change, although the difference was statistically insignificant. The 5-year disease-free survival rates of the group in which the stage did not change and of the group in which the stage changed from III (fifth edition) to IVA (sixth edition) were 64% and 34%, respectively ( $P = .08$ ). Local recurrence was more frequently observed in the group in which the stage changed from III (fifth edition) to IVA (sixth edition).

**Conclusion:** The new AJCC staging system seems to be more accurate in predicting the survival rates for patients with advanced but surgically resectable sinonasal squamous cell carcinoma (stage IVA).

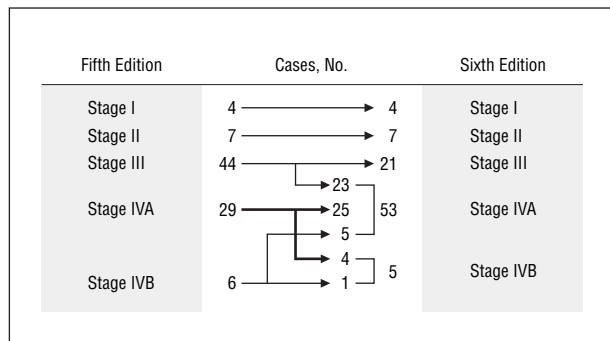
*Arch Otolaryngol Head Neck Surg.* 2007;133:131-134

**S**INONASAL MALIGNANT TUMORS comprise 3% of all malignant tumors of the head and neck.<sup>1</sup> Neck node metastasis occurs in only about 7% to 15% of malignant tumors, and distant metastasis is also very rare compared with other head and neck cancers. Therefore, the successive control of local recurrence of the tumor is extremely important for treatment success.<sup>2</sup> The American Joint Committee on Cancer (AJCC) published the sixth edition of the staging system in 2003.<sup>3</sup> In the fifth-edition staging system of sinonasal cancer, surgically resectable tumors and nonresectable tumors were all grouped together in the T4 stage, which made it difficult to evaluate the results of surgery. Furthermore, according to one study of the fifth edition of the AJCC staging system, that system may be inappropriate for presuming the prognosis of the disease compared with the 1997 Union Internationale Contre de Can-

cer (UICC)-AICC staging system.<sup>4</sup> In the revised sixth edition, such points were considered, and some cases underwent stage changes. For the maxillary sinus, T4 lesions have been further divided into T4a (resectable) and T4b (unresectable) lesions, leading to the division of stage IV into stages IVA, IVB, and IVC. These changes were mostly from the new T stage, including adjustment of involved sites. If the new staging system works, there must be some points of difference in survival rates and local recurrence rates between stage changing and unchanging groups. We tested the new AJCC staging system against the survival rates of patients with sinonasal cancers and investigated the characteristics of the patients whose stages were changed. Although there are many histopathological types of sinonasal cancers, for better comparison we focused exclusively on sinonasal squamous cell carcinoma. This study was conducted to assess the effectiveness of the sixth edi-

#### Author Affiliations:

Department of Otorhinolaryngology—Head and Neck Surgery, Seoul National University College of Medicine, Seoul (Drs Lee, Hur, Jin, Rhee, and Min); Department of Otorhinolaryngology, College of Medicine, Pusan National University, Pusan (Dr Roh); and Department of Otorhinolaryngology, College of Medicine, Chungnam National University, Daejeon (Dr Rha), South Korea.



**Figure 1.** Stage changing from the fifth to the sixth edition of the American Joint Committee on Cancer staging system.

tion of the AJCC staging system by comparing survival rates of patients with sinonasal squamous cell carcinoma according to the criteria of both fifth and sixth editions of the staging system. This study shows that there is a decreased survival rate and an increased recurrence rate for patients with stage IVA tumors when the criteria of the sixth edition are applied to sinonasal squamous cell cancer. It is reasonable to speculate that local recurrence is a key factor that brings about these tendencies. Poor prognosis in patients with advanced carcinoma with a high T stage may also be attributable to this factor. It seems preferable to use the sixth edition for sinonasal cancers for predicting the survival rate for patients with advanced but surgically resectable tumors.

## METHODS

A retrospective study was undertaken with 113 patients histopathologically diagnosed as having squamous cell carcinoma of the sinonasal tract. These patients were treated at several hospitals in South Korea (including the Department of Otorhinolaryngology–Head and Neck Surgery, Seoul National University Hospital, Pusan National University Hospital, Chungnam National University Hospital, and Chungbuk National University Hospital) from September 1988 through August 2003. Of these patients, 90 who were followed up for at least 12 months were included in the study. To check the recent status of patients who had been lost to follow-up, telephone interviews and a review of the national cancer registry were conducted. There were 66 men and 24 women, resulting in a male-female ratio of 3:1. The mean age of the patients was 51 years (range, 32–80 years). The follow-up period was defined as the duration from the day of the beginning of treatment to the day the patient died or the day of the last visit or interview. The mean follow-up period was 45 months (range, 12–207 months).

The criteria revised from the fifth edition to the sixth edition are as follows: A new site has been added for inclusion into the staging system. In addition to maxillary sinus, the nasoethmoid complex is also described as a second site with 2 regions within this site: the nasal cavity and ethmoid sinuses. The nasal cavity region is further divided into 4 subsites: the septum, floor, lateral wall, and vestibule. The ethmoid sinus region is divided into 2 subsites: the right and left. The T staging of ethmoid lesions has been revised to reflect nasoethmoid tumors, and appropriate description of their T staging has been added. For the maxillary sinus, T4 lesions have been divided into T4a (resectable) and T4b (unresectable), leading to the division of stage IV into stage IVA, stage IVB, and stage IVC. When

the skin of the cheek, infratemporal fossa, pterygoid plate, and anterior orbital contents have been invaded, the T stage changes from T3 to T4a. When the orbit apex, skull base, and nasopharynx have been invaded, the T stage changes from T4 to T4b. If the N2 stage exists, the former stage IVB changes to IVA. In all cases, the stage was reevaluated by applying the criteria of the fifth and sixth editions of the AJCC staging system and by consulting the readings of preoperative radiologic images.

An observation of the stage changes is as follows: in 23 cases, stage III lesions were reclassified as stage IVA, and in 4 cases, stage IVA lesions were reclassified as stage IVB, all owing to changes in the T stage. In 5 cases, stage IVB lesions were reclassified as stage IVA, which was a result of changes of the N stage (**Figure 1**). Invaded areas that caused changes in the T stage were the infratemporal fossa in 15 cases, the pterygoid plate in 12 cases, the anterior orbital content in 6 cases, and the cheek skin in 4 cases. Involved sites in the nasal cavity were the maxillary sinus in 76 cases, the lateral wall of the nasal cavity in 8 cases, and the ethmoid sinus and the nasal septum in 6 cases. The ratio of left sites to right was 46:44.

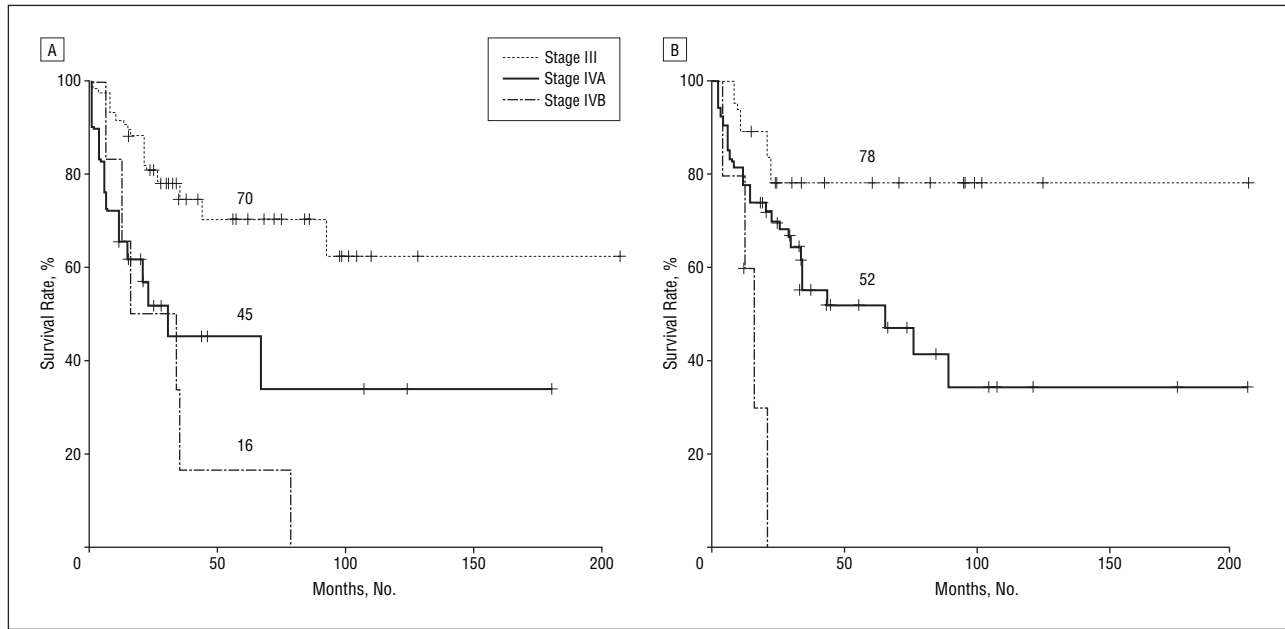
Twenty-seven patients were treated with surgery and radiotherapy; 17, with surgery only; and 3, with radiotherapy only. In 37 cases, patients received neoadjuvant chemotherapy; 23 received radiotherapy, 11 underwent surgery and radiotherapy, and 3 underwent surgery only. In other cases, 3 patients received chemotherapy; 1, palliative radiotherapy; and 2, conservative treatment only. In surgical cases, a total maxillectomy was performed in 26 cases, a partial maxillectomy in 22, a craniofacial resection in 4, a Denker operation in 3, and a Caldwell-Luc operation in 3.

A retrospective study was performed on the basis of clinical features, stages, treatment modalities, and recurrence. The disease-specific survival rates were analyzed according to both the fifth and sixth editions of the AJCC. The Kaplan-Meier analyses were used to compare stage-specific survival. Statistical significance was compared by a log-rank method and was considered significant when the *P* value was less than .05. We used SPSS software (version 12.0; SPSS Inc, Chicago, Ill) for statistical comparison.

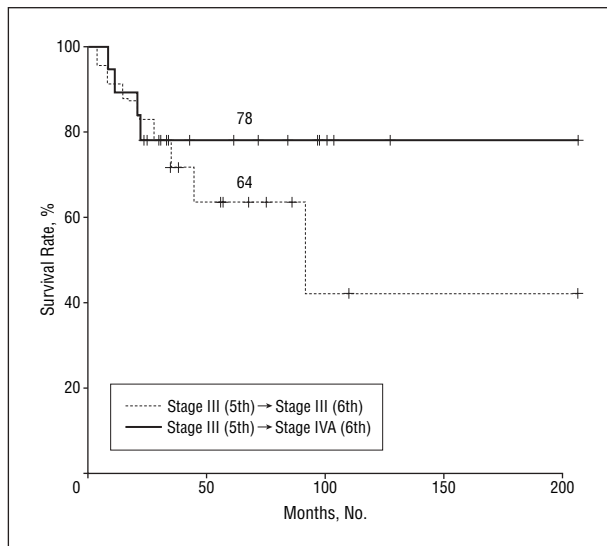
## RESULTS

According to the fifth edition, the 5-year survival rate at stage III was 70%, 45% at stage IVA, and 17% at stage IVB (**Figure 2A**). According to the sixth edition, the 5-year survival rate was 78% at stage III and 52% at stage IVA (**Figure 2B**). The survival rates in each group revealed significant differences.

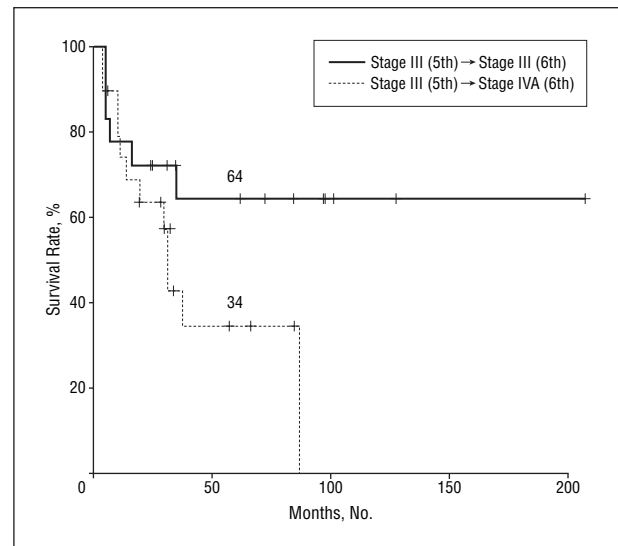
When the criteria of the sixth edition were compared with those of the fifth edition, the most distinct change was observed in stage III. The 5-year survival rate and disease-free survival rate according to the sixth edition were compared again by dividing the groups into those whose stages were reclassified from stage III in the fifth edition to stage IVA (23 cases) in the sixth edition and those whose stages were not changed (21 cases). The 5-year survival rates for each group was 64% and 78%, respectively (**Figure 3**), and the disease-free survival rates were 34% and 64%, respectively (**Figure 4**), which revealed a conspicuous difference. However, a statistical significance could not be determined. The recurrence feature was compared between the 2 groups. Recurrences were noticed in 7 of 21 cases in the group whose stage was not changed, and among them, 3 cases were local recurrences. Recurrences occurred in 11 of 23 cases in



**Figure 2.** Survival rates according to the fifth (A) ( $P=.001$ ) and sixth (B) editions of the American Joint Committee on Cancer staging system ( $P=.002$ ).



**Figure 3.** Comparison of survival rates between 2 groups that were changed from stage III (fifth edition [5th]) to stage IVA (sixth edition [6th]) and the unchanged stage III group ( $P=.34$ ).



**Figure 4.** Comparison of disease-free survival rates between 2 groups that changed from stage III (fifth edition [5th]) to stage IVA (sixth edition [6th]) and the unchanged stage III group ( $P=.08$ ).

the group whose stage was changed to stage IVA, and among them, local recurrences were noticed in 7 cases. The recurrence rates were 33% and 48%, respectively, with the latter group showing a higher local recurrence rate. When the group whose tumors were reclassified from stage IVA to IVB was compared with another group whose classification did not change from stage IVA in accordance with the sixth edition, the survival rate showed no difference ( $P=.19$ ).

#### COMMENT

Local recurrence following surgery occurs mostly in the posterior aspect of the maxillary sinus, periorbita, and skull base. It has been stated that ensuring a sufficient

resection margin in these areas is important.<sup>5</sup> Therefore, to obtain a sufficient resection margin, surgical approaches such as an infratemporal fossa approach or a transfacial approach are used at times. This demonstrates that applying a high T stage in cases where resection is difficult or impossible is appropriate, and such intent was implicated in the sixth edition.

Squamous cell carcinoma is the most common of the sinonasal malignancies.<sup>6</sup> It has been reported that 75% to 89% of tumors of the nasal cavity are of an advanced stage.<sup>5,7</sup> In this study, a similar aspect was observed; stage III and stage IV tumors comprised 88% of the lesions. A distinct increase in the number of stage IVA lesions was found when applying the criteria of the sixth edition. This may be due to the expansion of inclusion

criteria for stage T4a lesions in the new staging system. Early diagnosis of sinonasal malignancy is difficult because there are no early symptoms, most of its symptoms are similar to those of chronic rhinosinusitis, and a low prevalence rate of sinonasal malignancy makes it less likely to be suspected. In our study, neck metastasis was noticed in 9 of 90 patients at the time of presentation, which was similar to the rates of 8% to 18% found in other studies.<sup>8,9</sup>

It is already well known that male sex, old age, the T stage, the N stage, and the differentiation of the tumor are all factors independently related to the prognosis of the disease.<sup>7</sup> Because in 27 cases the T stage was changed and in 5 cases the N stage was changed when the criteria of the new edition of the staging system was applied, the changes in the survival rates were expected. When the maxillary cancer has invaded the pterygomaxillary and infratemporal fossa, the prognosis is worse than when the tumor is confined to the anteroinferior portion of the maxillary sinus because an en block resection is difficult.<sup>4</sup> This suggests that the prognosis for patients with stage T4a lesions according to the criteria of the sixth edition can be worse. In the study described herein, there were increased survival rates for patients with stage III and IVA lesions according to the criteria of the sixth edition compared with that of the fifth edition. This may be due to the exclusion in the sixth edition of T4a cases from stage III and T4b cases from stage IVA.

It has been reported that the 5-year survival rate of patients with sinonasal squamous cell carcinoma is 50%, that the recurrence rate is 56%, and that the prognosis is poor in cases of simultaneous invasion of multiple subsites.<sup>10</sup> Our study revealed similar results: a 60% 5-year survival rate and a 31% recurrence rate. There was a decreasing trend in the 5-year and disease-free survival rates in the group in which the stage was changed from III to IVA compared with the group whose lesions remained classified as stage III. However, we did not observe a statistical difference. This may be due to the early deaths of patients whose lesions were understaged in the group that remained at stage III and the relatively small sample size. For example, there was 1 patient in that group whose distant metastasis was found shortly after treatment. This problem is expected to be solved by further study with more cases. There was a difference in the recurrence rate, with 33% for the group whose lesions remained classified as stage III and 48% for the group whose stage was changed from III to IVA. The local recurrence rates were 44% and 64%, respectively. This difference in the recurrence rate may result in the decrease of survival in the group in which the stage changed from III to IVA according to the criteria of the sixth edition. Although our study was of a relatively small series of patients, it shows that there is a decreased survival rate and an increased recurrence rate for stage IVA when the criteria of the sixth edition of the staging system is applied to sinonasal squamous cell cancer. We can postulate that local recurrence is a key factor that brings about these trends, and local recurrence may also be a reason for poor prognosis in patients with advanced carcinoma with a high

T stage. We think that this study may help qualify the new staging system.

In conclusion, the sixth edition of the AJCC staging system for sinonasal cancer reflects the demand of up-staging locally advanced cancer that shows a higher recurrence rate and lower survival rate. There is a tendency for higher recurrence and lower survival rates when comparing the group in which the stage changed to IVA from III and the other group in which the stage did not change when the criteria of the new staging system was applied. The new staging system seems to be better at predicting the survival rate in the group with advanced but surgically resectable lesions (stage IVA).

**Submitted for Publication:** June 1, 2006; final revision received October 11, 2006; accepted October 23, 2006.

**Correspondence:** Chae-Seo Rhee, MD, Department of Otorhinolaryngology–Head and Neck Surgery, Seoul National University Hospital, 28 Yongon-dong, Chongno-gu, Seoul 110-744, Korea (csrhee@snu.ac.kr).

**Author Contributions:** Drs Lee, Hur, Rhee, and Min had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Lee, Hur, Roh, Rha, Jin, Rhee, and Min. *Acquisition of data:* Lee, Hur, Roh, Rha, Jin, Rhee, and Min. *Analysis and interpretation of data:* Lee, Hur, Rhee, and Min. *Drafting of the manuscript:* Lee, Hur, Rhee, and Min. *Critical revision of the manuscript for important intellectual content:* Lee, Hur, Roh, Rha, Jin, Rhee, and Min. *Statistical analysis:* Lee, Roh, Rhee, and Min. *Study supervision:* Lee, Rhee, and Min.

**Financial Disclosure:** None reported.

## REFERENCES

1. Osguthorpe JD, Richardson M. Frontal sinus malignancies. *Otolaryngol Clin North Am.* 2001;34:269-281.
2. Bhattacharyya N, Fried MP. Nodal metastasis in major salivary gland cancer: predictive factors and effects on survival. *Arch Otolaryngol Head Neck Surg.* 2002;128:904-908.
3. American Joint Committee on Cancer. *AJCC Cancer Staging Manual.* 6th ed. New York, NY: Springer-Verlag; 2003.
4. Cantu G, Mattavelli F, Pizzi N, Podrecca S, Valentini V. Malignant maxillary tumors involving the pterygo-maxillary and infratemporal fossae: a series of 65 patients and a comparison of the 1997 and 1977 UICC-AJCC staging systems. *Acta Otorhinolaryngol Ital.* 2000;20:100-105.
5. Bhattacharyya N. Survival and staging characteristics for non-squamous cell malignancies of the maxillary sinus. *Arch Otolaryngol Head Neck Surg.* 2003;129:334-337.
6. Bhattacharyya N. Factors affecting survival in maxillary sinus cancer. *J Oral Maxillofac Surg.* 2003;61:1016-1021.
7. Bhattacharyya N. Cancer of the nasal cavity: survival and factors influencing prognosis. *Arch Otolaryngol Head Neck Surg.* 2002;128:1079-1083.
8. Albright JT, Karpati R, Topham AK, Spiegel JR, Sataloff RT. Second malignant neoplasms in patients under 40 years of age with laryngeal cancer. *Laryngoscope.* 2001;111:563-567.
9. Gilliland FD, Hunt WC, Morris DM, Key CR. Prognostic factors for thyroid carcinoma: a population-based study of 15,698 cases from the Surveillance, Epidemiology and End Results (SEER) program 1973-1991. *Cancer.* 1997;79:564-573.
10. Fornelli RA, Fedok FG, Wilson EP, Rodman SM. Squamous cell carcinoma of the anterior nasal cavity: a dual institution review. *Otolaryngol Head Neck Surg.* 2000;123:207-210.