

Implication of Tumor Location for Lymph Node Metastasis in Maxillary Sinus Carcinoma: Indications for Elective Neck Treatment

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Purpose: For either neck irradiation or dissection, the indications for elective neck treatment (ENT) of maxillary sinus carcinoma are still unclear. The purpose of the present study was to investigate the relationship between the anatomic extent of the disease and lymph node metastasis in maxillary sinus carcinoma and to propose a recommendation regarding ENT.

Materials and Methods: In the present retrospective cohort study, patients with squamous cell carcinoma (SCC) and undifferentiated carcinoma (UDC) of maxillary sinus treated with radical intent from January 1995 to June 2015 in a single institution were recruited by retrospective medical record review. The demographic and tumor characteristics of the patients and maxillary sinus wall invasion, verified on pretreatment volumetric imaging studies, were analyzed. The Cox proportional hazards model was used to find the risk factors for nodal relapse, distant metastasis, and survival.

Results: Among a total of 71 identified patients, 66 had SCC and 5 had UDC. In 55 patients with node-negative disease, the risk of ipsilateral nodal relapse was 25.1% without ENT. In contrast, no ipsilateral nodal relapse was reported after ENT. On multivariate analysis, no chemotherapy (hazard ratio [HR] = 7.25; $P = .01$), posterior wall invasion (HR = 6.51; $P = .03$), and local failure (HR = 6.42; $P = .02$) were identified to be the risk factors of nodal relapse. Nodal relapse influenced the risk of distant metastasis with marginal significance (HR = 3.95; $P = .07$) but did not have an effect on survival. The most common regions of lymph node metastasis, at both initial presentation and relapse, were ipsilateral levels I and II.

Conclusions: For SCC and UDC of the maxillary sinus with posterior wall invasion, ENT involving ipsilateral levels I and II is recommended. Future studies with larger numbers of patients are needed to validate our conclusion.

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J Oral Maxillofac Surg ■:1-9, 2016

Received from Seoul National University College of Medicine, Seoul, Korea.

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This research was supported by the National Research Foundation of Korea, which is funded by the Korean government (Ministry of Education, Science, and Technology, Grant 2015059349), the Korean Health Technology R&D Project, Ministry of Health & Welfare, Republic of Korea (Grant H114C3459), and the National

R&D Program through the Dong-nam Institute of Radiological & Medical Sciences funded by the Ministry of Education, Science, and Technology (Grant 50595-2015).

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Received June 6 2016

Accepted October 2 2016

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0278-2391/16/30946-6

<http://dx.doi.org/10.1016/j.joms.2016.10.004>

Cases of maxillary sinus carcinoma are rare, with an annual incidence of less than 1 per 100,000 people in the United States.¹ Locoregional treatment of maxillary sinus carcinoma is challenging, owing to the presence of critical adjacent structures, especially the orbit. Furthermore, most patients will present with locally advanced disease,² because early symptoms resemble common nasal complaints and are sometimes completely absent. From the results of several retrospective studies, surgery is the mainstay of treatment,³⁻⁷ although radical radiotherapy with or without combined chemotherapy can be administered to patients with unresectable tumors or those who refuse surgery.⁸

In contrast, no consensus has been reached regarding the treatment of regional lymph nodes owing to the significant heterogeneity of the results from previous studies.⁹ Some researchers have not supported the use of elective neck treatment (ENT), either neck dissection or irradiation, in patients with node-negative (N0) maxillary sinus carcinoma. Reviews by Giri et al,⁴ Pezner et al,¹⁰ and Homma et al¹¹ reported nodal relapse rates of 8, 17, and 10%, respectively, in patients with N0 squamous cell carcinoma (SCC) who did not receive ENT and concluded that ENT might not be necessary. However, other studies have reported a relatively high rate of nodal relapse, 20% or greater, in patients with SCC and undifferentiated carcinoma (UDC).¹²⁻¹⁴

The contrasting results might have resulted from the heterogeneity of lymph node metastases in maxillary sinus carcinoma. In head and neck carcinoma located at other sites, the tumor extent plays an important role in lymph node involvement. Therefore, we conducted a retrospective review of the patients treated at our institution to investigate the correlation between the anatomic extent of the disease and the presence of lymph node metastasis. Considering the posterior drainage pattern of lymphatics from the maxillary sinus,¹⁵ researchers have hypothesized that invasion to the posterior components of the maxillary sinus increases the risk of lymph node metastasis. The specific aim of the present study was to determine whether a relationship exists between the tumor extent, as well as other clinical factors, and lymph node metastasis, thereby aiding in the selection of patients who would be more likely to benefit from ENT.

Materials and Methods

STUDY DESIGN AND DATA COLLECTION

To address the research purpose, we designed and implemented a retrospective cohort study. The institutional review board of the Seoul National University Hospital (Seoul, Korea) approved the present study,

which followed the Declaration of Helsinki. The sample included all patients with biopsy-confirmed SCC and UDC of the maxillary sinus who had undergone radical treatment from January 1995 to June 2015 at Seoul National University Hospital (Seoul, Korea). Patients with evidence of distant metastasis at presentation were excluded. To evaluate the anatomic factors, we included those patients who had undergone computed tomography (CT) or magnetic resonance imaging (MRI) before treatment. Tumors from the nasal cavity and ethmoid sinus were excluded by defining the site of origin as the anatomic area with the greatest volume of the mass.

Patient information was collected by retrospective medical record review. The imaging studies of the patients were also reviewed completely. Using the imaging studies and surgical pathology reports, we restaged the disease of all patients according to the 2010 American Joint Committee on Cancer staging system.¹⁶ Tumor staging was based on pathologic examination; however, clinical staging was used when the patient had not undergone any surgery.

ANATOMIC CONSIDERATIONS

To find an association between the tumor extent and lymph node metastasis, we reasoned that representative anatomic variables should be easily and clearly determined using volumetric imaging studies and associated with the pattern of lymphatic drainage. With this perspective, we simplified the maxillary sinus to an upside down tetrahedron that consists of 4 walls defined anteriorly by the facial tissues, posteriorly by the infratemporal fossa, medially by the nasal cavity, and superiorly by the orbit. Invasion to the 4 walls of the maxillary sinus (ie, the anterior, posterior, medial, and superior walls) were selected as the representative anatomic variables and evaluated by 1 of us (S.H.J.) using all available pretreatment imaging studies. In the present review, invasion was defined as extension beyond the bony walls. Examples of wall invasion defined in the present study are shown in [Figure 1](#).

VARIABLES

The primary predictor variables were the tumor invasions to the walls of the maxillary sinus. Other demographic and tumor characteristics, such as age, sex, tumor histology, and stage, were analyzed as secondary predictor variables. The primary outcome was the time to nodal relapse, which was defined as the interval between the beginning of treatment and the detection of nodal recurrence either on imaging studies or physical examination. Secondary outcomes included overall survival and distant metastasis-free survival, which were defined as the interval between the beginning of the treatment and death, and the beginning of the

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