RESEARCH COMMUNICATION

# Prognosis of Gingival Squamous Cell Carcinoma Diagnosed after Invasive Procedures

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## Abstract

**Gingival squamous cell carcinoma (SCC) has a relatively poor prognosis, because differential diagnoses ofperiodontitis and osteomyelitis are difficult to exclude. As such, gingival SCC is usually diagnosed late, following invasive procedures such as extraction or curettage. The purpose of this study was to classify gingival SCC patients into two groups according to the location of their primary lesion: dentate and edentulous, and to determine the appropriate treatment strategy by comparing clinical and histological features as well as treatment results. The medical records of 76 patients diagnosed with gingival SCC andtreated at one institute from 1 January 1993 to 31 December 2007 were reviewed. The overall 5-year survival rate was 60.7%, and the mean survival was 98 months. Factors affecting survival included bone invasion of the primary lesion (p = 0.035), neck node metastasis (p = 0.001), and local recurrence (p = 0.000). The results suggest that more aggressive treatment, such as setting a broad surgical field and enforcing preventive neck dissection, can improve outcome, although they are associated with increased rate of cancer bone invasion and neck metastasis in patients diagnosed with cancer after receiving invasive procedures.**

**Key words:** Squamous cell carcinoma - surgery - mandibular neoplasms - maxillary neoplasms

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## Introduction

It is known that gingiva is rare site of involvement of oral squamous cell carcinoma (SCC) (Choi et al., 2006). Still, several authors reported that gingival SCC is the most common site of occurrence of oral SCC (Cho and Kim, 1992, Chung and Kim, 1990, Oh et al., 2009). Gingival SCC has a relatively poor prognosis, because the differential diagnoses, periodontitis and osteomyelitis, are difficult to exclude. As such, gingival SCC is usually diagnosed late, following invasive procedures such as extraction or curettage. Previous data (Kusukawa et al., 2000, Suzuki et al., 1998) suggest that the risks of gingival SCC recurrence, cervical lymph nodes metastasis, and distant metastases are increased in patients with history of tooth extraction. In our previous study (Hong, 2001), we found that tumor related with previous dental extraction or curettage tends to be more extensive than what was predicted from an imaging point of view. The result affected the surgical method of the patients who underwent invasive procedures such as extraction or curettage. The purpose of this study was to classify gingival SCC patients into two groups, according to the primary lesion: dentate and edentulous, to compare the clinical, histological features and treatment results, and to determine the appropriate treatment strategy.

## Materials and Methods

The records of patients who were diagnosed with gingival SCC and underwent surgical treatment at the Department of Oral and Maxillofacial Surgery, Dental Hospital, Yonsei University Medical Center from 1st January 1993 to 31st December 2007, and followed-up for more than 32 months were reviewed. The following cases were excluded: 1) Patients with history of previously treated head and neck cancers; 2) Patients with history of head and neck irradiation; 3) Patients with cancers primarily involving floor of mouth, buccal cheek, retromolar pad, tongue, and maxillary sinus and secondarily invading gingiva; 4) Patients who did not receive any surgical treatment because of distant metastases at initial diagnosis.

The following information from patient medical records were reviewed: age, sex, duration of symptom, site of primary lesion (maxilla or mandible), characteristics of primary site (dentate or edentulous), history of invasive procedures before diagnosis, histologic bone invasion of primary tumor, pathologic T stage, pathologic N stage, pathologic stage, surgery of primary site and neck node, radiotherapy, primary site recurrence, neck recurrence, distant metastasis, survival, and survival time. The control group was consisted of patients

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who did not receive invasive procedures. Duration of the primary symptoms was calculated based on the number of months the patients endured the symptoms continuously, from its first documentation to surgery. For example, patient diagnosed as SCC after tooth extraction with/without curettage on the primary site because of continuous discomfort was classified as patient received invasive procedures on dentate lesion, even though the patient presented edentulous state at the time of diagnosis. Disease stages were classified according to the TNM staging classification (American Joint Commission on Cancer, 2002, 6th edition) (O'Sullivan and Shah, 2003). Maxillary gingival SCC was not classified according to surgery of the primary lesion, but mandibular gingival SCC was classified as marginal mandibulectomy and segmental mandibulectomy including hemimandibulectomy for convenience. According to our previous study (Hong et al., 2001), segmental mandibulectomy was considered when tumor was suspected to invade the bone marrow radiologically in patients with history of previous extraction. According to neck dissection method, all were classified as selective neck dissection (level I, II, and/or III) or radical neck dissection including modified radical neck dissection. Elective neck dissection was opted in almost patients with mandibular gingival SCC, and patients with advanced stages of maxillary gingival SCC in accordance with the report by Lubek (2010).

*Statistical Analysis*

Survival rates were calculated using the Kaplan-Meier method with SPSS 18.0, and were compared by the Log-rank test with 95 percent confidence level. Patients were divided into two groups, depended upon whether invasive procedure was performed. The invasive procedures were tested for their effects on the primary lesion, cancer bone invasion, cervical metastasis, local recurrence, neck recurrence, and distant metastasis by the Pearson chi-square test with a 95% confidence level.

## Results

Seventy-six (n=76) patients were included in the study with a mean age of 59.7 years (range 33 -86 years). Male to female ratio was 2.45:1 (54 male: 22 female). Maxillary gingival SCC was present in 23 patients, mandibular gingival lesion was present in 53 patients. The primary lesion was classified as dentate in 45 patients, edentulous in 26 patients. Others lesions, such as peri-implant lesions in 2 patients, and multiple or large lesions deemed difficult to judge as dentate/edentulous in 3 patients. Forty-seven (n=47) patients experienced bone invasion of primary tumor. Marginal mandibulectomy was performed in 17 patients, segmental mandibulectomy in 36 patients. Neck dissection was performed in 62 patients, of whom 26 underwent radical neck dissection. Characteristics of gingival SCC patients according to pathologic stage are summarized in Table

**Table 1. Stage Distribution of Gingival Squamous Cell Carcinoma Patients**

| | | T stage | | | | Total |
|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4a | |
| N stage | 0 | 11 | 6 | 4 | 26 | 47 |
| | 1 | 0 | 2 | 0 | 10 | 12 |
| | 2a | 0 | 0 | 0 | 1 | 1 |
| | 2b | 2 | 4 | 0 | 9 | 15 |
| | 2c | 0 | 0 | 0 | 1 | 1 |
| Total | | 13 | 12 | 4 | 47 | 76 |

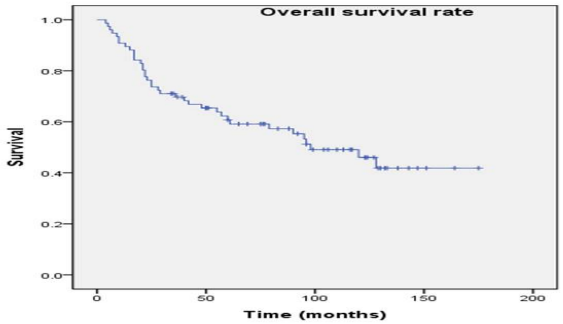


**Figure 1. The Overall Survival Rate of Gingival Squamous Cell Carcinoma Patients**

1. Local recurrence during the post-surgical follow-up period was found in 24 patients, neck recurrence in 8 patients, and 6 patients experienced distant metastases. The overall 5-year survival rate was 60.7%, and the mean survival was 98 months (Figure 1). Factors affecting survival included bone invasion of primary tumor (p = 0.035), neck node metastasis (p = 0.001), and local recurrence (p = 0.000).

**Table 2. Comparison of Characteristics and Treatment**

| | Invasive procedures 38 patients | No invasive procedures 38 patients | P-value |
|---|---|---|---|
| Duration of history | 6±4.73 | 5.6±11.53 | |
| Primary lesion‡ | | | |
| Dentate | 33 (73.3%) | 12 (26.7%) | 0.000 |
| Edentulous | 5 (19.2%) | 21 (80.8%) | |
| Bone invasion† | | | |
| O | 30 (78.9%) | 17 (44.7%) | 0.002 |
| X | 8 (21.1%) | 21 (55.3%) | |
| Neck node metastasis† | | | |
| Positive | 18 (47.4%) | 11 (28.9%) | 0.098 |
| Negative | 21 (52.6%) | 27 (71.1%) | |
| Mandibulectomy† | | | |
| Marginal | 8 (24.2%) | 9 (45.0%) | 0.117 |
| Segmental | 25 (75.8%) | 11 (55.0%) | |
| Neck dissection† | | | |
| No | 2 (5.3%) | 12 (31.6%) | 0.040 |
| Elective | 24 (63.2%) | 12 (31.6%) | |
| Radical | 12 (31.6%) | 14 (36.8%) | |
| Radiation therapy† | | | |
| Yes | 19 (50.0%) | 15 (39.5%) | 0.356 |
| Local recurrence† | 11 (28.9%) | 7 (18.4%) | 0.280 |
| Neck node recurrence† | 5 (13.2%) | 3 (7.9%) | 0.455 |
| Distant metastasis† | 3 (7.9%) | 3 (7.9%) | 1.000 |
| 5-year survival | 62.3% | 60.1% | 0.320 |

**Table 3. Comparison of Characteristics between 3 Groups of Patients with Gingival Squamous Cell Carcinoma**

| | Dentate + IP | Edentulous + IP | No IP | P-value |
|---|---|---|---|---|
| Bone invasion | | | | |
| Negative | | | | |
| No. | 8 | 0 | 21 | 0.005 |
| % | 24.2 | 0 | 55.3 | |
| Positive | | | | |
| No. | 25 | 5 | 17 | |
| % | 75.8 | 100 | 44.7 | |
| Neck metastasis | | | | |
| Negative | | | | |
| No. | 18 | 2 | 27 | 0.210 |
| % | 54.5 | 40.0 | 71.1 | |
| Positive | | | | |
| No. | 15 | 3 | 11 | |
| % | 45.5 | 60.0 | 28.9 | |
| Total No. | 33 | 5 | 38 | |
| % | 100 | 100 | 100 | |

IP, invasive procedure

The outcomes comparing patients who received invasive procedures against the control group are summarized in Table 2. Table 3 shows the difference between the three groups in this study.

## Discussion

According to Barasch et al. (1995), Overholt et al. (1996), Soo et al. (1988), and Eicher et al. (1996), gingival cancer is female dominant, or may not have a gender preference. Whereas, Choi et al. (2006), Kim and Kim (1996), Normura et al. (2001), and Shingaki et al. (2002) reported a male dominant tendency of gingival SCC. After this reports, it is suggested to analyze the cause of the male dominant tendency of gingival SCC in Asian patients.

It has been reported that factors affecting the outcome of gingival SCC included extraction history, primary tumor size, bone invasion, neck node metastasis, pathologic stage, perineural invasion, and negative surgical margins (Byers et al., 1981, Overholt et al., 1996, Soo et al., 1988). The hypothesis that history of previous extraction worsens prognosis was suggested by Peterson (1993), and neck node metastasis was more commonly found in patients who underwent extraction (Suzuki, 1998). It has been suggested that dissemination of cancer cells into the circulation during invasive procedures could increase the risks of distant metastases (Kusukawa et al., 2000). However, the association between survival and history of previous extraction remains controversial. This study was conducted to determine whether invasive procedures, such as extraction conducted prior to cancer diagnosis affected treatment outcome.

Of 45 patients diagnosed with gingival SCC on dentate lesion, 33 patients (73.3%) received invasive procedures, such as extraction or curettage (Table 2). This could be explained by the fact that gingival cancer in dentate site can mimic clinical and radiological features of periodontitis, such as chronic inflammation making the diagnosis of gingival SCC more complicated. In addition, the possibilities that chronic inflammation may cause cancer is suggested by several authors (Balkwill and Mantovani, 2001, Podilchak, 1961), even though it is in controversy up to recently.

The difference in neck metastasis ratio between the dentate and the edentulous group did not reach statistical significance, because only 5 patients were included in the group with invasive procedures on edentulous gingiva. However, bone invasion of tumor was seen in all patients who underwent invasive procedures for edentulous lesion, compared to 75.8% of patients who underwent invasive procedures for dentate lesion ($p = 0.005$); the remaining patients (24.2%) in the latter group were confirmed as not being bone invasion, because in this study, the invasive procedure included removal of floating teeth without curettage. This result suggests that removal of floating teeth without curettage may not disseminate the cancer cell into bone marrow.

Between the group that received invasive procedures and the control group (Table 2), there is little difference in the average duration of symptom, being 6 months and 5.6 months respectively. However, the standard deviation of the control group is higher, and it can be interpreted that patients who underwent invasive procedures were diagnosed and treated after a certain period, whereas duration of symptoms in the control group were more variable. Patients who received invasive procedures showed significantly higher risks of experiencing bone invasion ($p = 0.002$), and neck node metastasis remains insignificant ($p = 0.098$). Differences in tumor recurrence rate, cervical recurrence, distant metastasis and 5-year survival between the two groups were not statistically significant.

In this study, patients who underwent invasive procedures showed higher rate of primary tumor bone invasion than the control group, in contrast with Suzuki's conclusion (1998) that T stage was not affected by previous extraction. Because cancer bone invasion is known as predictive factor of survival (Byers et al., 1981, Oh et al., 2009, Soo et al., 1988), it was assumed that prognosis would be poorer in patients who underwent invasive procedures. However, when comparing patients who underwent invasive procedures with those who did not, there was no significant difference in primary lesion recurrence. It can be hypothesized that resection field in patients who received invasive procedures were set up more broadly, for instance, proportion of patients who received segmental mandibulectomy was 75.8% in the invasive procedure group, versus 55.0% of the control group in patients diagnosed with mandibular gingival SCC. However, in patients with maxillary gingival SCC, it was difficult to find any difference in surgical methods performed, due to the wider extension of the resection margins including all the invaded bone, and even the inferior wall of the maxillary sinus.

The difference of neck metastatic rate did not reach 95% level of significance between the two groups, but reached a difference at 90% level of significance. Radical neck dissection was performed in similar proportion in the two groups (31.6% vs. 36.8%), and selective neck dissection was performed more frequently in invasive procedure group (63.2% vs. 31.6%). It can be interpreted that preventive neck dissection was performed in patients who did not display obvious clinical evidence of cervical metastasis in the invasive procedure group. Radiation therapy was also more frequently performed on the invasive procedure group, but the difference did not reach significance.

As a result, invasive procedures performed on primary lesion affect the T and N stage of gingival SCC, but aggressive management, such as setting a broad surgical field or enforcing preventive neck dissection is thought to improve patient outcome, including neck recurrence and distant metastasis.

This study only included patients who underwent surgery, and excluded patients who already developed distant metastases at preoperative evaluation who subsequently did not undergo surgery. Therefore, it was only possible to compare patients on a defined postoperative distant metastasis endpoint, but not on the endpoint of preoperative distant metastasis. Consequently, the results of this study remain insufficient to refute Kusukawa's suggestion (2000) that dissemination of cancer cells increased the possibility of distant metastasis. In addition, the differences on such suggestion could be diminished, because we performed incisional biopsies in all patients before surgery.

There is the obvious confounding factor that patients who had teeth extraction probably did so because they had loosening of the teeth due to extensive medullary bone invasion and that these patients were therefore in a worse prognostic group than the group with no extractions because of the more aggressive bone invasion. But the histories of many patients include other invasive procedures such as curettage of extraction socket, which is suggestive to disseminate cancer cells.

The 5-year survival rate of maxillary and mandibular gingival SCC was reported as 62.41%, vs. 60.61%, respectively (O'Sullivan and Shah, 2003). These figures present poor prognosis, compared to SCC developed in other sites. The results of this study suggest that more aggressive treatment, such as setting a broad surgical field and enforcing preventive neck dissection can improve outcome, although they are associated with increased rate of cancer bone invasion and neck metastasis in patients diagnosed with cancer after receiving invasive procedures due to suspected periodontitis and osteomyelitis.

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