Oral Medicine/Original Research

Evaluation of infiltrative growth pattern in squamous cell carcinoma of the tongue: Comparison with Yamamoto–Kohama classification

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ABSTRACT

Objectives: In Japan, diagnostic differences between institutions/facilities and pathologists have led to discussions about reinvestigating the standards of diagnosis. Our objective was to reinvestigate the usefulness of these methods for assessing the recurrence risk of squamous cell carcinoma of the tongue.
Subjects and methods: Clinical and histopathological data from 168 patients with tongue squamous cell carcinoma were analyzed to compare two grading systems: the Yamamoto–Kohama (YK) classification and infiltrative growth pattern (INF).
Results: According to the YK classification, 5-year disease-free survival rate was significantly lower for grade 4C than for grades 1, 2, and 3 ($p < 0.05$). However, the 5-year disease-free survival rate did not differ significantly according to the INF. Grades 4C and 4D according to the YK classification did not have significantly different 5-year survival rates and did not differ to the corresponding INFc rate ($p = 0.652$). Furthermore, Cox's proportional hazards models did not identify any specific prognostic marker differences between patients with 4C and 4D tumors in relation to 2-year survival rates.
Conclusion: The INF classification did not demonstrate superiority over YK classification in assessing relapse risk in patients with squamous cell carcinoma of the tongue. We plan to further investigate the usefulness of INF grading for predicting recurrence risk by accumulating more cases.

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1. Introduction

Histopathological grading is an indicator of the malignancy of squamous cell carcinoma. One of the most common histological grading systems is the WHO grade classification (1971) [1] that is based on the Broders classification (1920) [2] for lip cancer, in which the degree of differentiation toward stratified squamous epithelium is mainly used as an indicator. This classification is customarily used worldwide because in large populations, it shows a correlation with prognosis or lymph node metastases; however, its usefulness is not high for individual cases. Therefore, some histopathological grading systems, including the Jakobsson classification (1973)

[3], the Willen classification (1975) [4], the Anneroth classification (1984, 1987) [5,6], and the Bryne classification (1995) [7], have been proposed. In these classifications, four to eight factors in the border of the tumor mass and the host tissues are rated, and the malignancy is evaluated by a total count. The usefulness of these grading systems has been tested in many studies but they are not in wide spread use because of the complexity of the systems. In Japan, particularly in the field of oral surgery, many institutions use the Yamamoto–Kohama (YK) classification [8–10], which is based on the Jakobsson classification and focuses on alveolar histology at the border of the tumor mass and the host tissues. In recent work, the WHO has pointed out that the grade classification has a low correlation with prognosis and that the mode of diffuse infiltration at the deep tumor border is important for prognosis [11]. However, recent institutional and diagnostician-based variations have been reported in diagnoses obtained using the YK classification, suggesting that a review of the diagnostic criteria is needed [12,13]. The YK classification was recently used to grade tumors in digestive regions such as the esophagus [14]. In addition, infiltrative growth pattern (INF), which is commonly used to grade malignant tumors in the digestive organs (e.g., the esophagus, stomach, and large
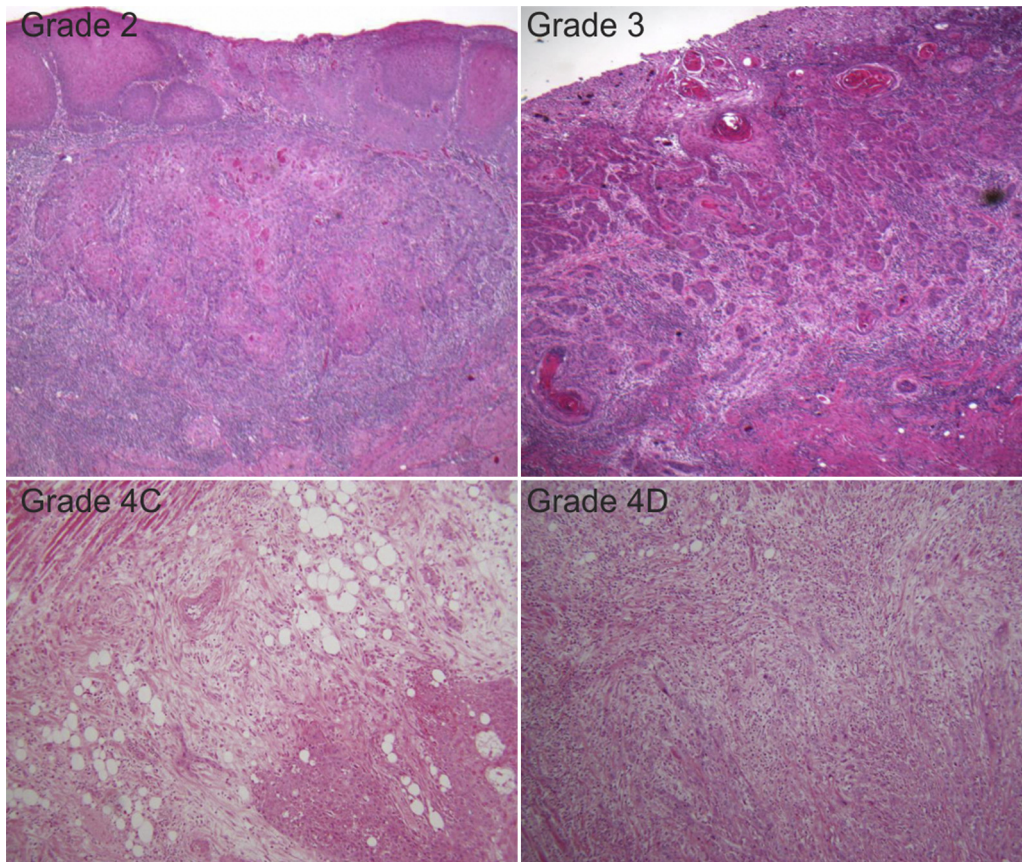
Fig. 1. Grade 2: cords, less marked borderline. Grade 3: groups of cells, no distinct borderline. Grade 4C: diffuse invasion of cord-like type. Grade 4D: diffuse invasion of diffuse, widespread type.

intestine), was recently applied to the oral region, and a correlation with the YK classification was suggested. The present study compared two methods of evaluating clinical, histopathological, and histopathological grading systems: the YK classification and infiltrative growth pattern (INF). Our objective was to reinvestigate the usefulness of these methods for assessing the risk of recurrence of squamous cell carcinoma of the tongue by evaluating patients who had undergone treatment at our institution.

2. Subjects and methods

2.1. Subjects

The subjects were 193 patients with tongue squamous cell carcinoma who had received treatment in the Oral and Maxillofacial Surgery, Tokyo Dental College between 2000 and 2010. Twenty-five patients with noninvasive cancer, in which the degree of invasion had not reached the muscular layer, were excluded because the parenchyma of the tumor was not clear.

For treatment, 70 patients (41.7%), 76 patients (45.2%), 5 patients (3%), and 17 patients (10.1%) underwent surgery alone, surgery plus chemotherapy, surgery plus radiotherapy, and surgery plus chemotherapy and radiotherapy, respectively.

All the specimens were histologically confirmed using microscopy with the operator blinded to each patient's clinical course.

2.2. Clinical evaluation

Tumor-Node-Metastasis (TNM) staging was performed according to the Union Internationale Contre le Cancer classification (2009) [15]. Staging of cervical lymph nodes was performed according to the General rules for Clinical and Pathological Studies on Oral Cancer: A Synopsis [16]. Clinical growth pattern was evaluated according to the Tongue Cancer Handling Guideline [17] produced by the Japan Society for Oral Tumors.

2.3. Histopathological evaluation

Resected specimens were analyzed by histopathological examination of hematoxylin and eosin staining of paraffin-embedded sections.

The diagnostic criteria using the YK classification were defined as follows: grade 1, the border line is well defined; grade 2, the border line is slightly disordered; grade 3, the border line is unclear, and small and large alveolar tumors are scattered; grade 4C, the
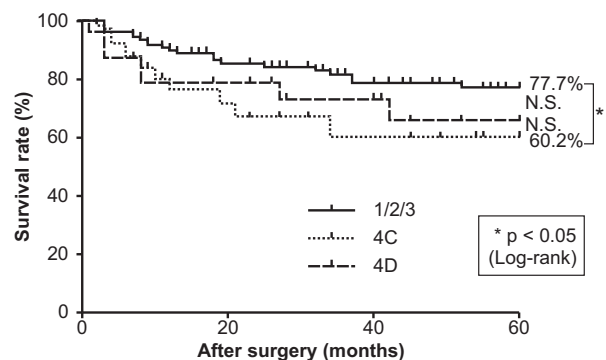

Fig. 2. Survival rates of patients with tongue cancer according to the YK classification using the Kaplan–Meier method.