Oral Science International xxx (2018) xxx–xxx

Contents lists available at ScienceDirect

Oral Science International

journal homepage: www.elsevier.com/locate/osi

Original Article

Risk factors in securing successful surgical resection of oral squamous cell carcinoma

Yoshitaka Nakanishi [a,b], Shin-ichi Yamada [a,*], Rishiho Nishizawa [a,b], Tetsu Shimane [a,c], Takahiro Kamata [a], Takeshi Koike [a,d], Shinobu Uehara [a,e], Hiroshi Kurita [a]

[a] Department of Dentistry and Oral Surgery, Shinshu University School of Medicine, 3-1-1, Asahi, Matsumoto, 390-8621, Japan
[b] Department of Oral and Maxillofacial Surgery, Asama General Hospital, Saku, Japan
[c] Department of Oral and Maxillofacial Surgery, Suwa Central Hospital, Chino, Japan
[d] Department of Oral and Maxillofacial Surgery, Ina Central Hospital, Ina, Japan
[e] Department of Oral and Maxillofacial Surgery, Shinonoi General Hospital, Nagano, Japan

ARTICLE INFO

Article history:
Received 2 November 2017
Received in revised form
27 December 2017
Accepted 28 January 2018
Available online xxx

Keywords:
Oral cancer
Squamous cell carcinoma
Surgical
Preoperative therapy

ABSTRACT

The purpose of this retrospective study was to analyze the factors that had a significant effect on securing a successful surgical resection (surgical margin) in oral cancer surgery. One hundred forty-eight consecutive patients who underwent planned radical resection of oral squamous cell carcinoma (SCC) were analyzed. Successful resection was judged if pathological examination of the surgical specimen revealed a clear surgical margin (no SCC within 5 mm, n = 116), while an unsuccessful resection was judged if there was a close and involved surgical margin (SCC within 5 mm, n = 21; and SCC at margin, n = 11). Univariate analyses showed that gender, age, and T-classification had significant influence on successful surgical resection. The results of multivariate logistic regression analysis showed that age (odds ratio [OR] = 1.042, 95% CI = 1.001-1.084), T-classification (OR = 1.656, 95% CI = 1.060-2.587), and the presence of preoperative treatment (OR = 2.868, 95% CI = 1.047-7.85) had significant effects on successful surgical resection. The results of this study suggested that successful resection of oral SCC was difficult in patients with either older age or advanced (T4) tumor. It is also suggested that preoperative therapy had a positive effect on securing a pathologically clear surgical margin.

1. Introduction

Surgical resection of the primary tumor with adequate margins is an essential component of the treatment strategy for patients with oral squamous cell carcinoma (SCC) because failure to achieve a clear surgical margin results in an increased risk of local recurrence and subsequently a poor prognosis [1–8]. Previous report has recommended a clinically clear surgical margin of more than 10 mm [9]. It has also been reported that the recurrence rate in cases with a pathologically clear margin of less than 5 mm was higher than the rate in those with a margin of more than 5 mm [10,11]. However, it is sometimes difficult to resect carcinoma with securing a sufficient clear margin (equal to or more than 5 mm of clear area around the tumor in the pathological specimen). Anatomical geography, clinical stage, pathological/biological behavior of the tumor, and skill of the surgeon, among others, might influence successful surgical resection of the tumor. In this study, therefore, we tried to analyze factors that influence unsuccessful surgical resection of oral SCC.

2. Patients and methods

2.1. Patients

This study protocol was approved by the Committee on Medical Research of Shinshu University.

In this study, the medical records of a series of 148 consecutive patients who underwent planned radical resection of their primary carcinoma with or without adjunctive radiotherapy and/or chemotherapy for previously untreated oral SCC at the Department of Dentistry and Oral Surgery, Shinshu University Hospital, between January 1990 and December 2007 were retrospectively reviewed. Data collection included gender, age, demographic information on tumors, TNM classification at diagnosis according to the 2002 sixth

* Corresponding author at: Department of Dentistry and Oral Surgery, Shinshu University School of Medicine, 3-1-1, Asahi, Matsumoto, 390-8621, Japan. Tel.: +81 263-37-2675, fax: +81 263-37-2676.
E-mail address: yshinshin@shinshu-u.ac.jp (S.-i. Yamada).

https://doi.org/10.1016/S1348-8643(18)30003-X
1348-8643/

edition of the American Joint Commission on Cancer TNM staging system [12], degree of differentiation [13], mode of invasion [14], preoperative therapy, and clinical response of preoperative treatment.

2.2. Treatment strategy

In author's institute, treatment strategies were selected depending on the tumor stage, medical conditions, performance status (PS), activity of daily life, and patient choice. Surgery is the preferred treatment for patients with oral cancer. Patients with a relatively good health condition (PS equal to or less than 2) underwent radical surgery with/without chemo/radiotherapy. In surgery, all primary tumors had been resected radically with curative intention, securing a clinical margin of more than 10 mm (superficial and deep margins). Patients who hesitated in accepting surgical intervention or who did not have surgery available because of a busy schedule were selected for preoperative chemo/chemoradiotherapy. During the period of preoperative chemo/chemoradiotherapy (CRT), patients were encouraged to undergo surgery after completion of preoperative chemo/chemoradiotherapy. All patients who received neoadjuvant chemotherapy (NAC) underwent radical surgery. The preoperative treatment strategy was chemoradiotherapy before 2000 and NAC after 2001. The chemoradiotherapy included external irradiation with 30–40 Gy of total doses combined with/without chemotherapy using cisplatin (CDDP) or 5-FU. The regimen of NAC consisted of a combination of CDDP-based multi drugs including CDDP + 5-FU, or CDDP + 5-FU+ docetaxel. In most patients, modifications in chemotherapy dosages were made for toxicity, as indicated using standard criteria. The preoperative CRT followed by surgery for advanced OSCC was reported to produce high clinical and histopathologic complete response and survival rates [15]. It is considered that, even in advanced oral cancers, it could be possible to avoid extended resection and perform minimally invasive surgery in which the extent of resection of primary tumor and neck is reduced to preserve morphology and function in patients who achieve a good response (CR and good PR in the primary tumor, CR in the neck) following preoperative CRT [15]. Therefore, the extent of surgery was not modified according to tumor responses to preoperative therapy, even in cases with complete response, and resection was performed for the initial-sized tumor. Surgery included the removal of the primary tumor, and radical neck dissection was performed in patients who had clinically positive cervical lymph node metastasis. Elective neck dissection was not routinely performed. Postoperative adjuvant radiotherapy with a dose field of more than 60 Gy was administered to patients with involved margins or extracapsular lymph node spread. Patients with recurrence that was considered potentially curable and operable underwent salvage surgery and radiotherapy. Patients with recurrence that was considered incurable were treated with palliative chemotherapy. In this study, the surgery was carried out by, or under the direct supervision of, experienced oral and maxillofacial surgeons with the board-certified specialist in oral and maxillofacial surgery of Japanese society of oral and maxillofacial surgeons. Intraoperative frozen-section analysis of clearance was used in almost all the patients. Based on the above-mentioned two systems, the difference in successful resection was reduced in this study.

2.3. Date analysis

Pathological assessment of surgical specimens was performed using the standardized pathological protocol comprising tangential sections of superficial margins and sagittal sections of deep surgical margins. An experienced pathologist and the responsible surgeon assessed all histological sections. The patients were classified into three categories according to the status of the surgical margin, which was assessed at the closest point to the surgical resection margin. The three categories of status of the surgical margin are as follows:

Clear: No evidence of microscopic carcinoma and dysplastic epithelium within 5 mm (≧5 mm) of the margin.

Close: Microscopic carcinoma or dysplastic epithelium within 5 mm (<5 mm) of the margin, but not at the margin.

Involved: Evidence of carcinoma at the margin in either an intraoperative frozen section or postoperative pathological assessment.

Successful radical resection was reported if a clear surgical margin was obtained in the pathological assessment of the surgical specimen. Meanwhile, unsuccessful resection was reported if there was a close or involved margin.

Univariate and multivariate analyses were carried out to analyze the factors that have a significant effect on successful radical resection of the primary tumor. Independent factors employed in the study were age, primary site, T-classification, N-classification, degree of differentiation, mode of invasion, presence or absence of preoperative treatment, and clinical efficacy of the preoperative treatment [16,17]. The Kaplan–Meier method was used to examine overall survival (OS) curves and local control curves (LCC). OS was defined as the time from the first visit to the occurrence of death from any causes including OSCC, and LCC as the time from the enforcement of local dissection to the occurrence of local recurrence. Differences between survival curves were examined by the log-rank test.

Statistical analyses were performed using the StatView software package for Macintosh (SAS Institute, Inc., NC, USA). All p values <0.05 were considered significant.

3. Results

One hundred forty-eight patients with primary oral SCC were included in the study population. The characteristics of these patients are shown in Table 1. The median age at diagnosis was 66 years (range 27–86 years). The most common primary site was the tongue (97 patients, 45.3%); 24 (16.2%) patients had lower gingival cancer, 21 (14.2%) upper gingival cancer, 20 (13.5%) buccal mucosa cancer, 15 (10.1%) oral floor cancer, and 1 (0.7%) hard palate cancer. Preoperatively, 92 patients underwent chemotherapy and/or radiotherapy. Clinical response to the preoperative treatment was evaluated using RECIST [15,16]. Of these patients, complete response was obtained in four (4.3%), partial response in 45 (48.9%), stable disease in 42 (45.7%), and progressive disease in one (1.1%).

Of the 148 patients, 116 (78.4%) had a clear surgical margin, 21 (14.2%) a close margin, and 11 (7.4%) an involved margin. Eight patients with an involved margin were assessed using intraoperative frozen sections, and supplemental resection margins were negative on final pathology. The other three patients were judged only after the final pathology and underwent no additional resection. In 8 patients with a positive margin in intraoperative analysis but clear in postoperative analysis, two patients showed local recurrence. Therefore, this might suggest the usefulness of intraoperative analysis to achieve a clear margin. Consequently, 116 patients were categorized as having a successful resection and the other 32 patients (21.6%) were categorized as having an unsuccessful resection on the basis of the pathological assessment of the surgical margin.

The 5-year OS rate of patients with a clear margin was 71.2%, and with a closed/positive margin, 58.1% (Fig. 1). However, there was no significant difference between these groups (Log-rank test: $P = 0.172$). The 5-year LCC rate of patients with a clear margin was

Please cite this article in press as: Nakanishi Y, et al. Risk factors in securing successful surgical resection of oral squamous cell carcinoma. Oral Sci Int (2018), https://doi.org/10.1016/S1348-8643(18)30003-X