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Comparative clinical outcomes of Taiwanese patients with resected buccal and tongue squamous cell carcinomas

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ABSTRACT

Objectives: Although patients with buccal squamous cell carcinoma (SCC) usually show acceptable outcomes, local control and survival rates are generally lower than those observed for tongue SCC. This study was designed to compare the clinical outcomes of Taiwanese patients with these two common oral cavity malignancies.

Methods: Patients with first primary buccal or tongue SCC who were included in the Taiwanese Cancer Registry Database between 2004 and 2012 were eligible. The study sample consisted of 16,379 patients (7870 buccal SCC and 8509 tongue SCC) who received surgery with or without adjuvant therapy. The 5-year disease-specific survival (DSS) and overall survival (OS) rates served as the outcome measures.

Results: Compared with tongue SCC, patients with buccal SCC had a higher prevalence of males (95.7% vs. 86.4%, $p < 0.0001$), pT4 disease (21.4% vs. 12.7%, $p < 0.0001$), and p-Stage IV (30.4% vs. 24.8%, $p < 0.0001$) but a lower frequency of pN2 disease (15.2% vs. 18.5%, $p < 0.0001$). The 5-year DSS and OS rates of buccal SCC patients were slightly higher than those of tongue SCC (78% vs. 77%, $p = 0.0297$; and 71% vs. 69%,

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p = 0.0231, respectively). Multivariate analysis identified tumor site (tongue vs. buccal SCC), sex (male vs. female), age (≥65 vs. <65 years), pT classification (T4/T3/T2 vs. T1), and pN classification (N3/N2/N1 vs. N0) as independent prognostic factors in the entire study cohort.
Conclusions: The survival advantage of buccal SCC over tongue SCC appears significant in large clinical samples, despite a higher prevalence of p-Stage IV disease in the former.

Introduction

Buccal squamous cell carcinoma (SCC) is rare in Western countries, representing approximately 10% of all oral cavity SCC [1]. However, its prevalence has been reported to be similar to that of tongue SCC in areas where betel quid chewing is endemic [2]. This phenomenon has been attributed to the well-known carcinogenic effect of betel quid chewing in the long-term [2]. The prevalence rates of betel quid chewing in Taiwanese males and females are 20.9% and 1.2%, respectively. In Taiwan, the significant sex-related differences in the frequency of tobacco and betel quid chewing may explain the higher incidence of oral cavity SCC in males (20.81 cases per 1 million persons) than in females (2.40 cases per 1 million persons). Moreover, the endemic use of betel quid chewing in our country may also account for the known differences between Taiwan and Western countries in terms of specific tumor subsites. Accordingly, 45–50% of Taiwanese patients with oral cavity SCC have tumors arising from the area classified as ICD-145 (buccal, retromolar and hard palate), whereas the prevalence of these neoplasms is significantly lower in Western areas [3]. Notably, engagement in risky oral habits – including betel quid chewing (80%), cigarette smoking (85%), and alcohol drinking (65%) – is common in Taiwanese patients with oral cavity SCC. Although acceptable outcomes for patients with buccal SCC have been reported [2–7], local control and survival rates are generally lower than those observed for tongue SCC [8–16]. Treatment of oral cavity SCC continues to rely on surgery, regardless of the anatomical site of origin. Subsequently, the use of adjuvant therapy is chiefly driven by the presence of specific postoperative pathological risk factors [17]. In light of the similar treatment approaches, we designed the current study to compare the clinical outcomes of patients with buccal SCC and tongue SCC in Taiwan (a betel quid chewing endemic area). To this aim, we reviewed the nationwide Taiwan Health Promotion Administration database made available as of 2004. We also sought to identify the main prognostic factors in these two patient groups and compare the outcomes of Taiwanese patients with buccal SCC with those previously reported in the published literature.

Patients and methods

Patients

A retrospective review of data gathered from the nationwide Taiwanese Cancer Registry was conducted. The registry can be openly accessed from all of the university hospitals in Taiwan through the Research Service Center for Health Information. The study protocol was approved by the Institutional Review Board of the Chung Gung Memorial Hospital (IRB number: 103-5976C). As of 2004, a nationwide Taiwan Cancer Registry Database (TCRD) "long-form" has been implemented. Differently from the previously available "short-form" database, the new dataset also comprises information on cancer stage, treatment approach, and tumor relapses. The registry has collected data from all of the major hospitals to which patients with a pathological diagnosis of oral cavity SCC are referred (covering >98% of all Taiwanese patients). Moreover, relevant data from the Taiwanese National Health Insurance Research Dataset were available.

Selection of the study patients

Patients who had buccal SCC or tongue SCC between 2004 and 2012 were eligible for this study. Specifically, we selected patients with the following International Classification of Diseases for Oncology, Third Edition [ICD-O-3] codes: tongue cancer [C02.0; C02.1; C02.2; C02.3; C02.8; C02.9] and buccal cancer [C06.0]. Monitoring was continued until December 2015. Fig. 1 summarizes the flow of the participants through the study. Patients were excluded when the following criteria were met: presence of an *in situ* carcinoma (n = 109) or previous history of cancer (n = 2477). Of the 20,454 patients initially identified, a total of 17,977 were deemed eligible (8712 with buccal SCC and 9265 with tongue SCC). We further excluded 842 patients with buccal SCC and 756 patients with tongue SCC because they did not receive surgery as their initial treatment. After these exclusions, the final study sample consisted of 16,379 patients (7870 with buccal SCC and 8509 with tongue SCC). The distribution of disease stage in the entire study cohort was as follows: p-Stage I, 5692 (35%) patients; p-Stage II, 3902 (24%) patients; p-Stage III, 2287 (14%) patients; and p-Stage IV, 4498 (27%) patients.

Study variables

The following variables were collected in all participants: sex, age at diagnosis, tumor subsite, pathological tumor classification, pathological nodal classification, pathological overall stage, and treatment approach. Data on tumor staging available from the Taiwanese Cancer Registry "long form" are based on the AJCC sixth edition staging guidelines [18]. Information on pre-operative risky oral habits (i.e., alcohol drinking, betel chewing, and cigarette smoking) and pathological risk factors (e.g., margin status, tumor depth, and neck nodal extracapsular spread [ECS]) has been made available in our nationwide data set as of 2011 only. Consequently, we did not include these data in the current analysis.

Statistical analysis

The duration of follow-up was defined as the time elapsed from the day of surgery to the day of death (or censored on the date of the last follow-up). Deaths were confirmed using the Taiwanese National Register of Deaths. The 5-year disease-specific survival (DSS) and overall survival (OS) rates served as the main outcome measures. Cumulative survival curves were plotted with the Kaplan-Meier method and compared with the log-rank test. Univariate and multivariate Cox proportional hazards regression models were used to identify the predictors of survival endpoints. The results were expressed as hazard ratios (HRs) with their 95% confidence intervals (CIs). In the study, the survival estimation and comparison were based on five-year status, not full time information. All calculations were performed with the SAS software, version 9.3 (SAS Institute Inc., Cary, NC, USA). Two-tailed p values <0.05 were considered statistically significant.