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Comparison of different comorbidity measures for oral cancer patients with surgical intervention: A longitudinal study from a single cancer center

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ABSTRACT

Objective: Several comorbid measures have been developed and demonstrated the predictive ability for cancer mortality. We conducted a retrospective study on oral squamous cell carcinoma (OSCC) patients to compare the Charlson comorbidity index score (CCIS) to the Elixhauser comorbidity index score (ECIS).

Methods: Newly diagnosed OSCC patients ($n = 232$) post major surgery with or without adjuvant therapy were identified from the cancer registry database between 2006 and 2011. Comorbidities present prior to the cancer diagnosis were obtained and adapted to the CCIS and ECIS. The prevalence of comorbid conditions and the influence on disease-specific survival (DSS) rate were calculated and analyzed by Cox regression model. The discriminatory ability of these two comorbid measures was evaluated by using the adjusted hazard ratio and Akaike information criterion (AIC) in a multivariate regression model. The prediction accuracy was assessed using Harrell's *c*-statistic.

Results: Most of the patients (93.5%) were male with a mean age of 54 ± 11 years and 77 of them (33.1%) had at least one comorbid condition. The ECIS was associated DSS, with an additional 10% increased risk observed for mortality for each increased score (HR, 1.10; 95% confidence interval [CI], 1.03–1.18) after adjusting with pathological risk features. However, the CCIS was not an independent prognostic factor for these patients. The ECIS increased discriminatory ability but the CCIS did not improve discrimination.

Conclusions: Comorbid conditions significantly influenced the clinical outcomes of patient with OSCC post major surgery. A higher ECIS was associated with worse disease specific survival

Abbreviations: OSCC, oral squamous cell carcinoma; CCIS, Charlson comorbidity index score; ECIS, Elixhauser comorbidity index score; DSS, disease-specific survival; AIC, Akaike information criterion; HR, hazard ratio; CI, confidence interval; ICD-9, International Classification of Diseases, 9th revision; AJCC, American Joint Committee on Cancer; NCCN, National Comprehensive Cancer Network.

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indicative of a valuable prognostic indicator. The ECIS may be considered in further clinical trials for a variety of cancers, including head and neck cancers.

1. Introduction

Oral squamous cell carcinoma (OSCC) is among the 10th most common forms of cancer and is becoming more common across the globe, specifically in Western and Asian countries [1]. In Taiwan, the incidence of OSCC has continued to increase and is the fourth most common cause of cancer-related mortality among men [2]. Smoking, alcohol, and betel quid are well-known risk factors for oral cancer [3,4]. Besides the carcinogenic effect, these substances may also be associated with other systemic comorbidities, such as cardiovascular, pulmonary, metabolic disorders, chronic hepatitis, liver cirrhosis, and peptic ulcers [5,6]. The primary treatment modality for OSCC is major surgery with or without adjuvant therapy. These coexisting comorbidities may damper the treatment outcomes in these patients besides TNM stage and treatment modality [7,8].

Several measures have been developed to quantify comorbid conditions, including the Charlson et al. [9], and Elixhauser et al. [10] comorbidity classification which were presented in our analysis. The Charlson comorbidity index score (CCIS) derived from weight score for 19 medical conditions has been extensively used to evaluate the impact of comorbid conditions in a variety of cancers and non-cancer conditions [11–13]. The Elixhauser method, a more recently developed approach encompasses 30 comorbid conditions and was validated in acute-care inpatient hospital settings using administrative data [10]. In recent years, several studies have suggested that the Elixhauser method is a better comorbidity risk-adjustment model [14,15]. Moreover, a modification of the Elixhauser comorbidity measures has been developed by van Walraven et al. and uses a summation score to predict in-hospital mortality [16]; the use of this Elixhauser comorbidity index score (ECIS) has not been examined in a clinical cancer setting.

The present study uses a Cancer Registry Database in a single Cancer Center and focused on estimating the incidence of comorbid conditions and their impact on the management of OSCC patients post surgical intervention. A secondary objective was to compare these two different indices via the CCIS and ECIS for predicting the outcomes in these patients.

2. Materials and methods

2.1. Ethics statement

This study was approved by the Institutional Review Board of Buddhist Dalin Tzu Chi General Hospital in Taiwan. Review board requirements for written informed consent were waived because all personal identifying information was removed from the dataset prior to analysis

2.2. Patient demographics and database

The data for this study were collected from the Cancer Registry Dataset from the Buddhist Dalin Tzu Chi General Hospital Cancer Center from 2006 to 2011. The electronic medical records and cancer registry dataset were retrospectively reviewed in detail. Patients with newly diagnosed OSCC who received radical surgery with or without adjuvant therapy in this cancer center were included in this analysis. Patients who received neoadjuvant therapy or palliative intent (i.e., non-radical surgery due to advanced or widespread disease at diagnosis) were excluded. Cancer diagnoses and comorbid conditions were recorded based on the International Classification of Diseases, 9th revision (ICD-9) codes. Comorbidities (i.e., hypertension or diabetes mellitus) present prior to the major surgery of oral cancer were recorded. A total of 232 primary oral cancer patients with a histopathological diagnosis of squamous cell carcinoma were included in this study and whose primary care and medical records were also identified. The Cancer Registry Dataset included the date of diagnosis, site of the primary oral tumor, age, gender, margin status (positive or negative), differentiation (i.e., well, moderate, and poor), presence of perineural, lymph-vascular invasion, presence of extra-capsular spread, chemotherapy regimen, radiotherapy dosage, cause of death, clinical TNM stage, and pathological TNM stage. All patients were staged according to the American Joint Committee on Cancer (AJCC) classification system (7th edition). The administration of adjuvant therapy, if needed, was recommended based on national comprehensive cancer network (NCCN) guidelines and pathological findings, such as surgical margin, advanced T or N classification, perineural/vascular invasion, and extra-capsular spread. The clinical endpoint was the 2-year disease-specific survival (DSS) rate.

2.3. Comorbidity assessment and analysis

Comorbid medical conditions were graded for severity using the: (1) Charlson comorbidity index score (CCIS) and (2) Elixhauser comorbidity index score (ECIS). Comorbid condition information was obtained from medical records consisting of physician notes and discharge summaries up to the date of surgery by the primary author. The CCIS developed by Charlson et al. was used to quantify baseline comorbid conditions [9,11]. The CCIS is a weighted measure that incorporates 19 different medical categories, each of which is weighted according to its potential impact on mortality (Supplementary Table 1). The weight assigned to each comorbid condition ranged from 1 to 6 and all these conditions contributed to the final score calculated for each patient. Elixhauser et al. used sets of individual ICD-9-CM diagnosis codes to identify categories of comorbid conditions. A total of

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