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# Primary intraosseous squamous cell carcinoma of the mandible: locoregional control and survival is significantly reduced if the tumour is more than 4 cm in size

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## Abstract

To establish the prognostic factors for primary intraosseous squamous cell carcinoma we designed a retrospective study of patients treated in the head and neck department of a tertiary referral centre in China from 2010–2015. We collected clinical, radiological, and histopathological data from 36 patients treated during the given time period, among which 34 were followed up. There were 22 male and 12 female patients, 13 of whom gave a history of smoking tobacco and four who drank alcohol. All 34 patients were treated by segmental mandibulectomy and neck dissection. Nine had cervical lymph node metastases on histopathological examination, and none had invaded surgical margins. Twenty-eight were treated with radiotherapy postoperatively. During follow up nine died of locoregional recurrence or metastases. Specific factors such as cervical lymph node metastases were related to a greater likelihood of locoregional recurrence. Patients who drank alcohol were also more likely to develop metastases postoperatively. Tumours more than 4 cm in size were significantly associated with reductions in locoregional control and survival.

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**Keywords:** Primary intraosseous squamous cell carcinoma; Prognostic factor; Locoregional recurrence; Metastasis

## Introduction

Primary intraosseous squamous cell carcinoma (SCC) is a rare cancer of the head and neck that occurs mainly in the maxilla and the mandible, and is thought to originate

from the remnants of odontogenic epithelium.<sup>1–9</sup> It was first named intra-alveolar epidermoid carcinoma by Loos in 1913.<sup>6</sup> The World Health Organization (WHO) renamed it primary intraosseous carcinoma in 1972.<sup>10</sup> In 2005, WHO categorised it into three subtypes: solid tumours, SCC that arose from odontogenic keratocysts, and SCC that arose from other benign epithelial odontogenic tumours.<sup>11,12</sup>

The diagnostic criteria are strict: the lesion must be differentiated from other malignant tumours that invade the mandible. Metastatic tumours from distant sites, sinus carcinoma, and other odontogenic tumours must be identified precisely and excluded.<sup>3–6</sup>

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Primary interosseous SCC is a subgroup of oral cancers that is by default staged as stage IV by the Union for International Cancer Control (UICC) and the American Joint Committee on Cancer (AJCC) because of bony involvement, and irrespective of size. Clinical studies are needed to substantiate or challenge the current staging to give a meaningful perception of survival during follow up. The clinical and pathological features are not well understood as there are only a few published papers that have either described a small series or a single case report.

In this study we have retrospectively analysed the cases of primary interosseous SCC from the database of a single tertiary referral hospital to establish the prognostic factors.

## Patients and methods

Patients who were operated on at the department of oral and maxillofacial head and neck oncology in our hospital during 2010–15 with a diagnosis of mandibular primary intraosseous SCC were included in the study, and clinical, radiological, and histopathological data were collected. The histopathological diagnosis was confirmed by two experienced pathologists. The mean (SD) duration of follow up was 42 (19) months for surviving patients, and the minimum follow up period was 12 months.

All the tumours were staged according to the staging system of the AJCC,<sup>13</sup> so all patients were staged as TIVa or TIVb. The stages of lymph node metastases were classified accordingly. The maximum diameter of the tumour was calculated according to the radiological image and the size of the gross specimen. The other pathological factors were stratified according to standards of pathological appraisal.<sup>14</sup>

## Statistical analysis

We used descriptive statistical analysis, including Fisher's exact test to calculate the significance of differences in locoregional recurrences, metastases, and overall survival. Factors for which the probability was significant or approaching significance were added to the multivariate analysis with Cox's regression. The 1–5 year overall survival depending on different factors was also calculated. Kaplan–Meier survival curves were drawn to study the survival distributions, and the log rank test used to calculate the significance of the differences. Kaplan–Meier graphs were produced for all the important prognostic factors, and probabilities of less than 0.05 were accepted as significant.

## Results

A total of 3407 patients with oral cancer were recorded during the given time period, only 36 of whom fulfilled the inclusion criteria and were diagnosed as primary interosseous SCC. Two were lost to follow up. The data of the remaining 34

Table 1

Personal, clinical, and histopathological details of all patients, and those followed up.

| Variable                          | All patients | Number followed-up |
|-----------------------------------|--------------|--------------------|
| Site of tumour:                   |              |                    |
| Mental                            | 1            | 1                  |
| Body                              | 26           | 24                 |
| Ramus                             | 9            | 9                  |
| Age (years):                      |              |                    |
| ≤30                               | 0            | 0                  |
| 31–60                             | 25           | 23                 |
| >60                               | 11           | 11                 |
| Sex:                              |              |                    |
| Male                              | 24           | 22                 |
| Female                            | 12           | 12                 |
| Smoking:                          |              |                    |
| Yes                               | 15           | 13                 |
| No                                | 21           | 21                 |
| Alcohol:                          |              |                    |
| Yes                               | 5            | 4                  |
| No                                | 31           | 30                 |
| Initial operation:                |              |                    |
| Yes                               | 33           | 31                 |
| No                                | 3            | 3                  |
| Size of tumour (cm):              |              |                    |
| ≤4                                | 23           | 21                 |
| >4                                | 13           | 13                 |
| Neck dissection (levels):         |              |                    |
| I–III                             | 20           | 20                 |
| I–IV                              | 6            | 5                  |
| I–V                               | 10           | 9                  |
| Lymph nodes:                      |              |                    |
| Invaded                           | 10           | 9                  |
| Clear                             | 26           | 25                 |
| Reconstruction:                   |              |                    |
| Primary closure                   | 2            | 2                  |
| Flap:                             |              |                    |
| Adjacent                          | 5            | 5                  |
| Fibular                           | 15           | 14                 |
| Anterolateral thigh               | 3            | 3                  |
| Pectoralis major musculocutaneous | 11           | 10                 |
| TNM grade:                        |              |                    |
| T4N1M0                            | 4            | 4                  |
| T4aN1aM0                          | 2            | 2                  |
| T4bN1aM0                          | 1            | 1                  |
| T4bN1bM0                          | 1            | 1                  |
| T4N2M0                            | 6            | 5                  |
| T4aN2aM0                          | 2            | 2                  |
| T4aN2bM0                          | 2            | 1                  |
| T4bN2aM0                          | 1            | 1                  |
| T4bN2bM0                          | 1            | 1                  |
| T4N0M0                            | 26           | 25                 |
| T4aN0M0                           | 13           | 12                 |
| T4bN0M0                           | 13           | 13                 |
| Histopathological stage:          |              |                    |
| I                                 | 7            | 7                  |
| II                                | 18           | 17                 |
| III                               | 11           | 10                 |

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