

Clinical Diagnostic and Therapeutic Perspectives in Oral Cancer

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Citation: Ioannis Chatzistefanou, Martha Pyraki, Vassilis Petsinis. Clinical Diagnostic and Therapeutic Perspectives in Oral Cancer. Annal of Otol Head and Neck Surg. 2026;5(5):1-3.

Received Date: 16 July, 2026; **Accepted Date:** 18 July, 2026; **Published Date:** 19 July, 2026

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ABSTRACT

Oral squamous cell carcinoma (OSCC) has had an overall survival rate of 50% the last forty years. Delays in diagnosis constitute the main reason for the high mortality rates, because patients present with advanced-stage disease that is characterized by high tumor burden and regional lymph nodes, often demanding advanced and expensive treatment modalities. As a result, prognosis can be refined by early detection of OSCC, with clinical examination, imaging, biopsy, and multidisciplinary tumor board reviews that recruit the optimal therapeutic modalities for each patient (surgery, systemic therapy, radiotherapy). Finally, cervical lymph node status is an important prognostic factor in patients with OSCC, often indicating elective or modified radical neck dissections, combined with a minimum five-year follow-up, avoiding recurrences.

Key words: Oral cancer; Neck dissection; Unknown primary; Neck metastasis; Occult metastasis

DIAGNOSIS

With over 370,000 new diagnoses and 177,000 deaths annually, oral squamous cell carcinoma (OSCC) constitutes a global public health issue and represents 90% of oral malignancies [1]. In the last forty years, the 5-year mortality has been almost unchanged at 50%, driven by the fact that 50% of the patients with OSCC present initially with advanced stage disease [1]. 5-year overall survival rates are 80% for early-stage and 50% for advanced-stage OSCC, requesting implementation of a complex, expensive combination of treatments [2]. In advanced stages, malignant cells of OSCC tend to metastasize to the regional cervical lymph nodes, a fact correlated with depth of invasion (DOI) [3]. The American Joint Committee on Cancer (AJCC) has incorporated DOI into T staging, characterizing lesions as T2 when DOI is greater than 5mm, setting a threshold below 5mm for a lesion to be classified as early-stage OSCC [4].

Therapeutic outcomes are in danger when delays in diagnosis occur, due to patients' delay in seeking healthcare advice, inefficient healthcare systems, and time-consuming diagnostic algorithms [5]. Additionally, the differential diagnosis of early-stage OSCC is challenging because lesions such as leukoplakia, erythroplakia, frictional keratoses, and oral lichen planus should be excluded, while chronic ulcers that persist for more than two weeks after removal of any possible traumatic cause demand a biopsy [5]. Imaging protocols that mainly consist of contrast-enhanced computed tomography (CE-CT) and magnetic resonance imaging (MRI) should be implemented as staging modalities

before biopsy [6]. 18-fluorodeoxyglucose (FDG)-PET/CT is used in advanced stages, with a detection ability of lymph nodes of 4mm, also useful for second primary tumours in the upper airway, distant metastases, and recurrences [7]. An incisional biopsy is performed in most cases after completion of imaging to obtain a definitive histopathologic diagnosis [8]. A multidisciplinary tumor board comprising head and neck surgeons, radiologists, oncologists, and pathologists evaluates oncologic patients to determine the optimal therapeutic plan for each case of OSCC [9].

TREATMENT

The primary therapeutic strategy is surgical resection for early and advanced-stage OSCC, with a variety of restorative modalities from primary closure to free flap reconstruction, depending on the size of the defect [10]. An oncological resection requires 1 cm to 2 cm of macroscopically healthy soft- and hard-tissue margins, respectively [11]. Histopathologic examination classifies the margins as negative (more than 5mm), close (2-5mm), or positive (less than 2mm), or existing high-grade dysplasia, carcinoma in situ, or invasive carcinoma [11]. Close margins require strict observation during follow-up, while adjuvant chemoradiotherapy is demanded when positive margins or extracapsular nodal extension are observed, indicating advanced locoregional disease with high risk for recurrences and survival withdrawal [12].

OSCC's crucial prognostic factor is cervical lymph node involvement, with the aforementioned imaging modalities (CE-CT, MRI) and occasionally ultrasound-guided fine-needle aspiration cytology (US-FNAC) contributing to staging if definitive diagnosis cannot be made with non-interventional imaging [13]. In clinically node-negative necks (cN0), there is a risk of 15-20% for occult disease, especially when greater than 3 mm depth of invasion (DOI) is referred in the primary OSCC, with the performance of an elective neck dissection in cervical levels I to III offering regional disease control similar to modified radical neck dissection [13]. A long-term (at least 5 years), meticulous follow-up protocol should be implemented in patients who completed their individualized treatment as dictated by the multidisciplinary team board, every two months for the first two years, and every three to six months thereafter, mainly with clinical examination and endoscopy, and baseline post-treatment imaging at 3 to 4 months and after that whenever an indication of recurrence or second primary lesion occurs [14].

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