




# Prediction of Occult Lymph Node Metastasis in Early Tongue Cancer

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Tongue cancer has a relatively high occult lymph node metastasis (OLNM) rate of 24.4%, even in early stages (T1–T2), and cervical lymph node metastasis is significantly correlated with poor clinical outcomes [1,2]. Therefore, the prediction and treatment of cervical lymph node metastasis are important, even in patients with early-stage tongue cancer. A recent systematic review concluded that elective neck dissection (END), compared with observation, in T1–T2 early tongue cancer could significantly reduce locoregional failure and increase the disease-free survival (DFS) rate [3]. Nonetheless, in light of the risk of side effects and complications after END, detailed preoperative criteria for patient selection will be required.

The National Comprehensive Cancer Network guidelines recommend END or sentinel lymph node biopsy for neck management in early tongue cancer cases when the depth of invasion (DOI) of the primary tumor is greater than 3 mm, given the risk of OLNLM [4]. Although DOI and the worst pattern of invasion are currently used as predictive models for OLNLM in oral cancer, applying those criteria to actual preoperative evaluations is problematic because they are based on postoperative pathological results. Preoperative DOI measurements using imaging tests such as magnetic resonance imaging or intraoperative ultrasonography have been reported to have relevance to the postoperative pathological results; however, there are practical limitations in accurately assessing the DOI of small lesions using radiological methods [5]. A recently introduced deep learning-based modeling method can increase the prediction accuracy of OLNLM, but it is difficult to apply this model in the real clinical field consid-

ering time and cost [6]. Therefore, in addition to the above indicators, it is necessary to discover new markers for preoperative OLNLM prediction.

Lee et al. [7] recently reported the significance of defensin-associated genes as predictors of OLNLM in early tongue cancer. The authors performed RNA sequencing on primary tumor samples from 35 tongue cancer patients and analyzed differentially expressed genes (DEGs) according to OLNLM status in samples after END. Their analyses confirmed that lower expression of defensin-associated genes (*DEFB4A*, *DEFB103B*, and *DEFB4B*) in the primary tumor could be associated with an increased risk of OLNLM in early tongue cancer, suggesting that those genes could be used as biomarkers [7]. Another study published by the same author found that the expression of actin-associated genes such as *ACTA1* had a significant relationship with regional metastasis in early tongue cancer [8]. Yang et al. [9] reported that the expression of *TNFRSF10C*, a gene involved in immune-related pathways, had a significant relationship with OLNLM and DFS, and that the log<sub>2</sub> ratio of copy number variation of the gene could suggest a favorable prognosis in patients with node-negative early tongue cancer.

In early tongue cancer, preoperative biomarker-based OLNLM prediction for the primary tumor may provide more precise information regarding neck management. Nonetheless, it is questionable whether specific genetic information can be accurately confirmed from a small specimen obtained from a punch biopsy before surgery, and another limitation is that an accurate cut-off value for whether to perform END based on the level of marker expression has not yet been determined. Consequently, it is thought that the practical application of genetic biomarkers in the clinical setting will be possible in the future when technological advances are made to reduce the time and cost required to confirm DEG results before surgery in early tongue cancer patients.

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## CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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