

Analysis of Relationships between Degree of Tumor Invasion, Lymph Node Metastasis, and Substances Related to Metastasis in T1 and T2 Oral Tongue Cancer

Se-Heon Kim, M.D., Nam Hoon Cho, M.D., Jin Seok Lee, M.D.,
Young-Ho Kim, M.D., Eun Chang Choi, M.D., Kwang Moon Kim, M.D.
Department of Otorhinolaryngology, Yonsei University College of Medicine, Seoul, Korea

Introduction : Since T staging only depends on the size of tumor in early tongue cancer, we have to take account the depth of tumor invasion to predict LN metastasis and to decide on the extent of surgery. The objective of this study is to define factors related to tumor invasion in early tongue cancer hypothesizing that destruction of cellular matrix and neovascularization has its role in tumor invasion.

Method : 40 early T1, T2 stage tongue cancer patients who received radical surgery and neck node dissection was followed up for 4 years. To discover the invasion process in early tongue cancer, we observed the expression of substances related to extracellular matrix destruction (MMP2, MMP9), and substance related neovascularization (VEGF) using immunohistological method. We quantified the amount of neovascularization by dying CD 31. Most severe site of tumor invasion into the normal tissue was measured and labeled as depth of invasion. We analyzed the relationship between tumor invasion depth and expression of each substance, and also analyzed disease free survival and percentage of LN mets.

Result : In the group where there was presence of LN metastasis, the average depth of tumor invasion was $14.2 \pm$

5.25 mm, and in the group where there was no mets, the depth was measured to be 7.6 ± 5.05 mm, showing a statistically significant difference ($p=0.007$). There was no difference of tumor depth invasion whether there was expression of MMP2 and MMP9 or not. On the other hand, VEGF expression had a meaningful difference: In the group with VEGF expression, the average depth of tumor invasion was 12.2 ± 5.97 mm, compared with 7 ± 4.62 mm measured in group with no VEGF expression ($p=0.002$). Tumor with VEGF expression had average density of microvessels of 19.3 ± 5.21 , compared with 12.3 ± 4.66 in tumor with no VEGF, suggesting that VEGF expression and density of neovascularized vessels have direct positive relationship ($p<0.001$). The disease free survival was also significantly longer in patient with no VEGF expression ($p=0.019$).

Conclusion : Depth of tumor invasion has significant relation between expression of VEGF and density of neovascularization, and when VEGF expression was present, the chance of LN metastasis increased, and disease free survival of patients decreased significantly.