SURGICAL MANAGEMENT OF LOCALLY ADVANCED ORAL CAVITY CARCINOMA WITH NONSURGICAL INSIGHT AND FUTURE DIRECTIONS

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Objectives: Approximately 500.000 new cases of oral cancer (OSCC) are diagnosed each year worldwide. Due to the high mortality it is suffice to say that the prognosis is poor. At present, from the procedural aspect, III and IVa stage tumors represents an important challenge in maxillofacial surgery. It may cause losses of many essential functions due to the extensive destruction of the complex head and neck anatomy. Wide surgical margins in initially massive tumors require immediate reconstruction. Also, we aimed at investigating the association of TP53 gene pathogenic mutations with survival and response to cisplatin chemotherapy, as well as variant rs9344 in CCND1 gene in the susceptibility and prognosis of OSCC patients.

Methods: We retrospectively reviewed stage III and IV patient charts over the period of the last 5 years. All patients were admitted to the Clinic for Maxillofacial Surgery at the Military Medical Academy in Belgrade. Patients had resection of the stage T3 and T4 oral cancer performed combined with bilateral neck dissections, followed by facial reconstruction with microvascular free flaps and pedicled musculocutaneous flaps. The current study for CCND1 single nucleotide polymorphism included 104 OSCC patients and 107 healthy individuals without a cancer history and exons 4-8 of TP53 gene mutations were investigated in tumor tissue of 82 HPV-negative OSCC patients.

Results: All patients successfully recovered from the surgery. In addition, they received postoperative radiation and chemotherapy. Few patients had early postoperative complications but recovered during hospitalization. Patients have been closely followed for up to four years. Patients with pathogenic TP53 mutations had significantly shorter survival time and GA and homozygous mutated AA genotypes for the rs9344 polymorphism are associated with an increased oral cancer susceptibility.

Conclusions: Radical en-bloc resection remains the mainstay of treatment. The chosen reconstructive technique mostly depends on the extent and functional characteristics of the involved tissue. Polymorphism rs9344 in the CCND1 gene could be a potential

molecular risk factor for OSCC susceptibility, but not for disease prognosis. Pathogenic TP53 mutations could be a prognostic marker of reduced overall survival and poor response to cisplatin chemotherapy.