

Reconstruction of oral defects, using Bichat fat pad flap. Clinical and pathological study

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The main oral defects that need surgical reconstruction are produced by the excision of primary malignant tumors. The oral squamous cell carcinoma represents the primary malignant tumor of the oral cavity, representing 5-8% of all the cancer forms identified until now.

It is associated with high morbidity and mortality rates worldwide, because it is usually diagnosed in advanced stages, given the lack of symptoms and the versatility to mimic numerous lesions in the early stages.

Moreover, a rise in HPV-related oro-pharyngeal squamous cell carcinoma cases has been noticed, but it's involvement in non-oro-pharyngeal squamous cell carcinomas is still unknown.

Regarding the surgical treatment, the challenge is to perform an adequate closure of the defect. Because of the complexity of the oral cavity, even small defects may heal improperly and determine different degrees of impairment. That is why, surgeons try constantly to improve the surgical techniques by identifying the most suitable flaps for oral reconstruction.

The present study aims to evaluate the role of different parameters encountered in oral squamous cell carcinoma patients, as individual prognostic factors regarding the unfavourable evolution of this malignancy, respectively: dimension of the primary tumor, tumor grade, excision margins, positive to negative lymph nodes ratio (LNR), perineural invasion, neutrophil to lymphocyte ratio (NLR).

In addition, this study analyses the most frequently used flaps for oral defects, including those induced by oral carcinoma excision and to determine which has the best outcome. The focus of the investigation is the Bichat fat pad flap, a pedicled encapsulated adipose tissue with constant volume, which can be harvested intraorally and used for the closure of the oral defects located in the posterior part of the oral cavity. Because of the impressive dedifferentiation capacity of the adipose cells and of the individual vascularization, this flap can be used even in case of previously failed attempts, or in case of immunocompromised patients (Diabetes mellitus, history of radiotherapy) and it can be used for small- to medium-sized defects (up to 6 cm in diameter).

Also, because there is little to no information regarding non-oro-pharyngeal HPV-related oral squamous cell carcinomas and its role in modelling the tumor microenvironment, this study tries to establish the interactions between actin binding proteins such as Mena (mammalian Ena), vasodilator-stimulated phosphoprotein (VASP), and Ena-VASP-like, that have been shown to disrupt the actin cycle and promote tumor cell invasions and adhesion, and adhesion molecules E-cadherin and β -catenin, but also their possible correlation with alpha-smooth muscle actin (SMA), a marker of cancer-associated myofibroblasts.

To perform these investigations, I used the medical records of the patients diagnosed with oral squamous cell carcinoma and oral defects, treated in the Oral and Maxillo-Facial Clinic of Targu Mures during 2014-2020. I also performed the reconstruction surgeries using Bichat fat pad flap and followed the evolution of the patients, between 2018-2020. The databases created were used to perform the statistical part of the paper using Graphpad Instat3, Prism8,10, Medcalc and different tests in order to determine the significance of the findings, Kaplan Mayer survival analysis, Mann Whitney test, Fisher test, chi square test, ROC curve analysis.

Cases were processed following approval from the Ethical Committees of the Clinical County Emergency Hospital (no 32647/13.12.2018) and George Emil Palade University of Medicine, Pharmacy, Science and Technology of Targu-Mures, Romania (no 1777/10.06.2022). Signed informed consent forms for surgical resection and publication of clinicopathological data were obtained from all the patients.

For the first study, I included 299 oral squamous cell carcinoma patients, diagnosed and treated between 2014-2020. After the exclusion criteria 172 cases remained to be assessed. Using the Kaplan Mayer survival curves I investigated the impact of several parameters, dimensions of the primary tumor, tumor grades, depth of invasion, resection margins, perineural invasion, neutrophil to lymphocyte ratio, on the general survival of the patients.

Results show that the resection margins, the perineural invasion and the neutrophil to lymphocyte ratio are individual factors that have an unfavourable influence on the overall survival of the oral squamous cell carcinoma patients, thus they should be included in the stadialisation criteria of these malignant tumors. Further investigations regarding the NLR, using Man Whitney test showed correlation of this parameter with the advanced stages of the tumors but also with the tumor grades, in particular with the moderate differentiated oral squamous cell carcinomas.

The second study focused on two patient groups, the first group consisting of 79 patients diagnosed with oral squamous cell carcinoma defects, with different sizes and locations (infrastructure, midface-structure, pterygomandibular commissure, cheek mucosa) that were reconstructed using only Bichat flaps, or allowed to granulate secondarily or treated with combined methods. The purpose was to assess which method had the best outcome. Surgery was performed in 2019. The second group consisted from 140 patients diagnosed with oro-antral communications after various surgical procedures. For these patients I compared the outcomes of three flaps used for the surgical reconstruction, buccal flap, palatal flap and Bichat fat pad flap, in order to determine the best option. Surgery and assessment was performed between 2018-2020.

Results show for the first group that secondary granulation has the worst outcome, patients presenting speaking, eating and swallowing difficulties, retracting scars that affect the quality of life. Even small defects are prone to develop retracting scars and functional disabilities. The defects treated with or in combination with Bichat fat pad flap assured a better healing process with considerable less scarring or other difficulties.

For the second group I identified that the most used closure method for oro-antral communications was the buccal advancement flap which caused also the most complications. No dehiscencies were observed for the cases that used the Bichat fat pad flap, even in case of immunocompromised patients that had a history of radiotherapy. The second intervention performed for the relapsed cases favored also the Bichat fat pad flap, local conditions of the traumatised tissues being the possible explanation for these outcomes. Size defect also has an important role when choosing the reconstruction method and this study showed that medium sized defects require the use of a vascular well organised flap, which is the Bichat fat pad flap.

The third study evaluated 43 patients diagnosed with oral squamous cell carcinoma between 2018-2020. The purpose of this study was to evaluate the role of human papilloma virus (HPV) infections for the invasion and progression of the tumour and also to identify possible immunohistochemical markers involved in the epithelial-mesenchymal transition (EMT) of the non-oro-pharyngeal HPV positive oral squamous cell carcinomas.

Results showed that epithelial-stromal interaction may be mediated by the Mena/E-cadherin/SMA axis, which regulates interactions between tumor epithelial cells and stromal myofibroblasts, which is why further investigations of this pathway may determine more complex and individualised treatment options. Also, the HPV positive cases showed that loss of E-cadherin is associated with increased levels of Mena and SMA, finding consisting with the activation of the EMT, but also with a more aggressive invasion and evolution of the cases.

The reconstruction of postoperative defects and the management of the oral squamous cell carcinoma in general, requires a multidisciplinary approach in order to evaluate how surgery along with adverse prognostic factors affects both the quality of life and long-term survival outcomes.