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DIAGNOSTIC AND PROGNOSTIC VALUE OF miRNA IN ORAL CAVITY CANCER

Introduction:

Oral cancer is one of the most common malignancies along the world, constituting for about 3% of all malignancies. In 90% histopathologically it is squamous cell carcinoma (SCC). It is prognosed that within a few years it will be the most common death cause. Even though there are improvements in the diagnostics and treating protocols in recent years, the prognosis for patients with head and neck neoplasms remains poor. It is mostly dependent on the advancement of the disease while diagnosing, the occurrence of nodal metastases, micrometastases and the local recurrence after the primary treatment. In case of early detected neoplasms, the chance of curing is estimated at 90-95% while in advanced stage it drops to 20-35%.

Recent discoveries related to microRNA (miRNA) are giving a hope for a change in diagnostic and therapeutic approach and what is related – the improvement in treatment results (also for patients with head and neck neoplasms). miRNA is a short noncoding RNA, built out of 17-24 nucleotides. Its role is to post-transcriptive regulate gene expression and its target is messenger RNA (mRNA) in the region 3'UTR and 5'UTR (regions that do not translate). Binding to the target mRNA triggers translation inhibition or its degradation. It plays a crucial role in many cellular processes, for example in differentiation, proliferation, apoptosis, cell migration, oncogenesis and angiogenesis. The efforts of many researchers are aimed at defining the expression panel of different miRNA particles in patients with cancer. From 2005 there are many articles published, which aim to analyse the role of miRNA in cancerogenesis: its diagnostic and therapeutic potential, possibility to repair the DNA and the association between miRNA and HPV infection. It is suggested that defining the miRNA profile for cancers may be a predictive agent as well as prognostic and give a possibility to personalize the therapy.

Aim:

The aim of the investigation is to determine the diagnostic and therapeutic value of chosen miRNA (miR-21, miR-30a-5p, miR142-5p, miR-155-5p, miR204-5p) in oral squamous cell carcinoma (OSCC).

Research hypothesis:

miR-21, miR-30a-5p, miR142-5p, miR-155-5p, miR204-5p have diagnostic and therapeutic value in the treatment of OSCC.

Methodology:

Bioethical Committee Approval was obtained (no. RNN/228/21/KE). The approval of Hospital's Directors (WAM Hospital and Mikołaj Kopernik's Hospital) to access medical documentation was obtained.

Records of patients treated due to the oral cavity cancer were found (using ICD-10 classification: C00-04 and C06) in years 2009-2016. A patient database was created using inclusion and exclusion criteria.

The following data were obtained:

- Sex and age of the patient,
- Nicotinism and alcoholism,
- Localization of the primary tumor,
- Performed surgical treatment,
- Histological finding, including grading,
- Performed treatment,
- Numbers of histopathological paraffin blocks with primary tumor,
- Clinical TNM classification,
- Patient's follow-up and survival.

Control group: patients treated due to the chronic obturative dyspnea were selected that were treated with palatouvuloplasty. Post-operative material was examined histologically and described as a normotype oral mucosa.

Paraffin blocks and microscope slides were collected from the Department of Pathology of WAM Hospital. The analysis of the slides was performed to confirm the paraffin blocks containing primary tumor.

The same procedure was performed for M. Kopernik's Hospital.

The paraffin blocks were cut using microtome at width of 3µm and sent to the CoreLab Medical University of Łódź to perform the main part of the experiment.

For the analysis, the following miRNA were chosen: miR-21, miR-30a-5p, miR-142-5p, miR-155-5p, miR-204-5p. miRNA was isolated from the paraffin blocks using protocol "High pure miRNA isolation kit" from Roche. Single-column procedure was performed.

The expression level of miRNA was estimated using mercury LNA, miRNA Probe PCR kit from Qiagen.

The obtained data will be statistically analysed to find the correlation between chosen miRNAs and its diagnostic and therapeutic value in oral cavity cancer.

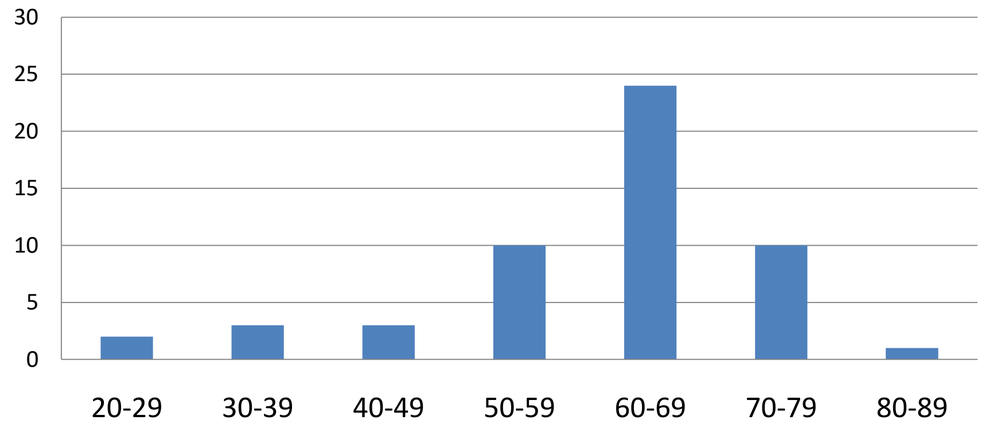

Fig.1. Age distribution of the patients. The highest incidence of OSCC was observed in the 6th and 7th decade of life.

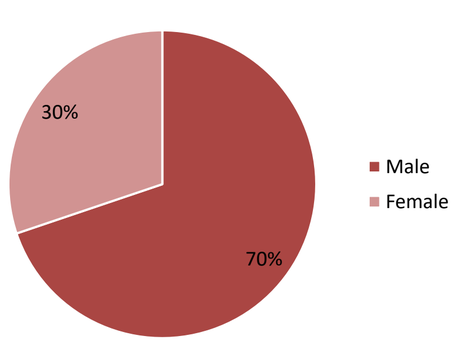

Fig.2. Gender distribution of the examined group.

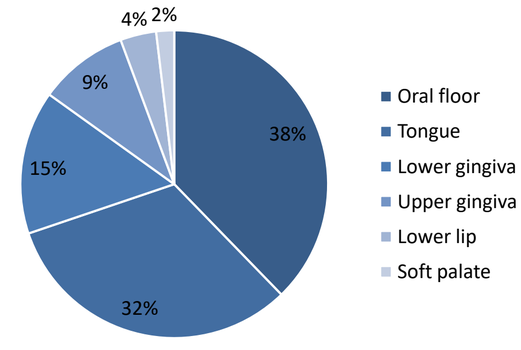

Fig.3. Localization of the primary tumor.

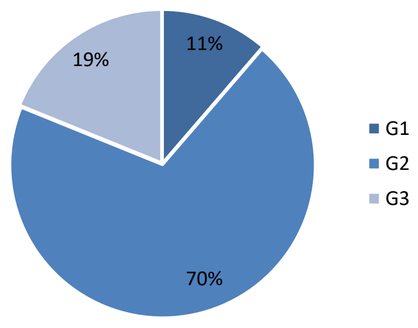

Fig.4. Neoplastic grading of the SCC.

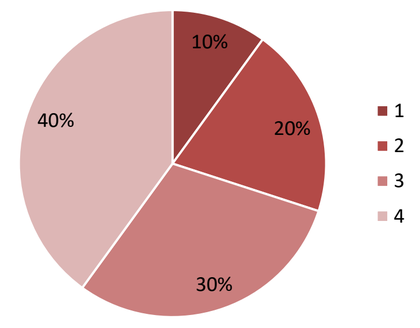

Fig.5. AJCC scoring.

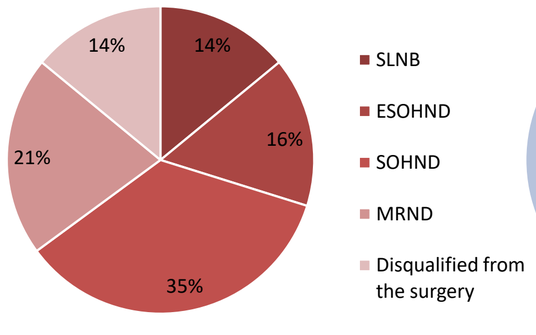

Fig.6. Lymphadenectomy performed.

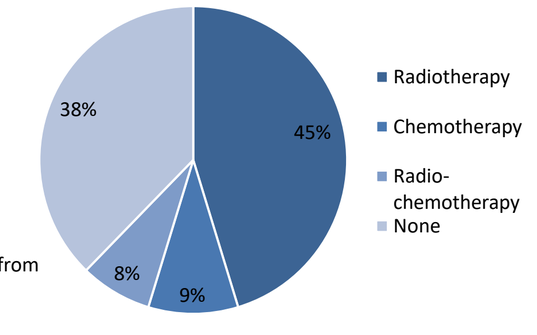

Fig.7. Performed adjuvant treatment.

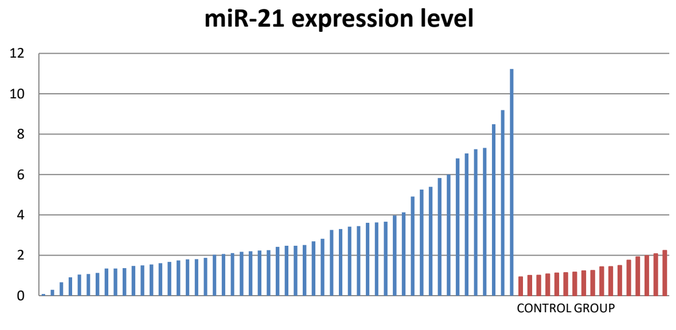

Fig.8. miR-21 expression level comparison. Control group is highlighted. It is seen that the expression of miR-21 is higher in the OSCC than in the control.

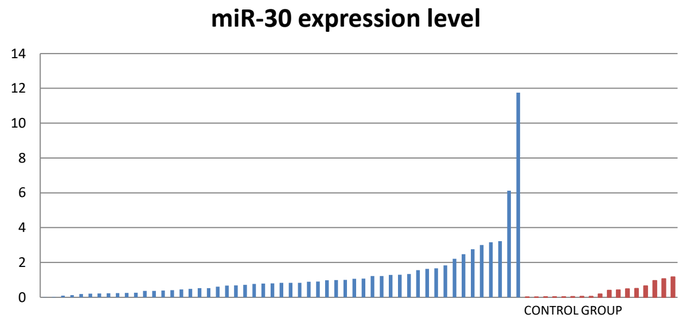

Fig.9. miR-30 expression level comparison. Control group is highlighted. It is seen that the expression of miR-30 is higher in the OSCC than in the control.

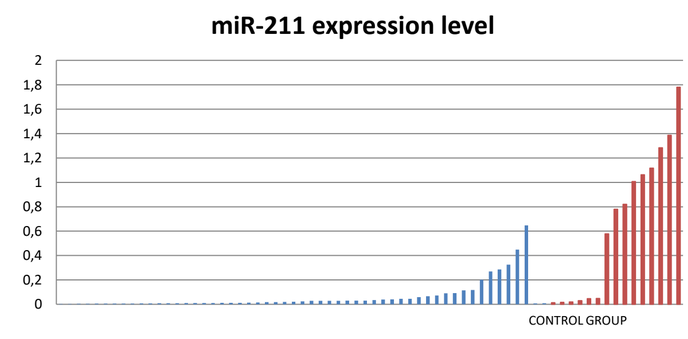

Fig.10. miR-211 expression level comparison. Control group is highlighted. It is seen that the expression of miR-211 is lower in the OSCC than in the control.

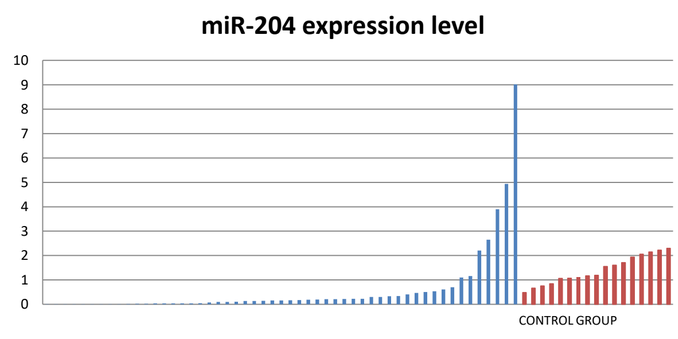

Fig.11. miR-204 expression level comparison. Control group is highlighted. It is seen that the expression of miR-21 is most cases lower in the OSCC than in the control.

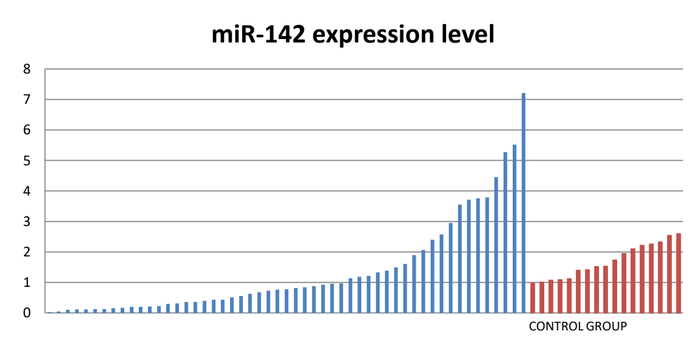

Fig.12. miR-142 expression level comparison. Control group is highlighted. It is seen that the expression of miR-142 is varying in the OSCC compared to the control.

Conclusion:

Comparing the control group with examined group there are seen different concentration levels of chosen miRNAs. Higher concentration of miR-21 and miR-30 is observed in patients with neoplastic disease compared to the control group. Lower values of the concentration level in the examined group were noted in miR-142, miR-211 and miR-204. The next step of the examination is the statistical analysis and the correlation of the miRNA expression level with the clinical course.