Streszczenie rozprawy doktorskiej w języku angielskim (Abstract of the doctoral thesis in English)

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Title of the dissertation: *Assessment of the concentration of vitamin D, melatonin, biomarkers of oxidative stress, inflammation and endocrine activity of adipose tissue in patients with head and neck cancer*

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Abstract:

Head and neck cancers (HNCs) are a rare group of oncological diseases. Despite significant advancements in medicine, HNCs remain a considerable clinical and social problem. More than 500,000 new cases of HNCs are diagnosed annually worldwide. HNCs affect various structures in the head and neck area, and their etiology is complex, involving environmental and genetic factors. The main predisposing factors for HNC include smoking and alcohol consumption. The symptoms of HNCs depend on the tumor's location and include pain, tissue ulceration, trouble breathing, difficulty swallowing and speaking, and enlarged lymph nodes in the neck for some patients. The primary treatment methods for HNCs include surgery and radiotherapy, which involve the use of ionizing radiation. During HNCs, there is an imbalance between the generation of reactive oxygen species (ROS) and the cells' ability to neutralize them. In a state of homeostasis, the body maintains a balance between the production of ROS and their scavenging through enzymatic and non–enzymatic antioxidant mechanisms. Antioxidant enzymes include superoxide dismutases (SODs), catalase (CAT), and glutathione peroxidases (GPxs), while non–enzymatic antioxidants comprise vitamins A, C, E, glutathione (GSH), and melatonin. In recent years, scientists have highlighted the antioxidant role of vitamin D. One of the main mechanisms linking obesity and cancer is chronic inflammation, which may become a source of ROS. During obesity, the synthesis and secretion of adipokines, hormones of white adipose tissue, are disturbed. In obese patients, the adipokine profile is altered. Pro–inflammatory adipokines promote oxidative stress and affect carbohydrate metabolism.

The aim of this doctoral dissertation was to determine the level of melatonin and vitamin D, as well as the activity of selected antioxidant enzymes, the concentration of lipid

peroxidation markers, selected adipokines, factors regulating glucose homeostasis, and inflammatory markers in HNC patients. Additionally, the study aimed to establish the relationship between the above–mentioned parameters and the patients' age and body mass index (BMI) in the course of HNC.

The condition for qualifying a patient for the study was the diagnosis of primary, malignant HNC. The study material consisted of the venous blood samples collected from patients with HNC and from healthy controls. From the venous blood sample, a suspension of red blood cells for the determination of SOD–1, CAT, GPx activities and malondialdehyde (MDA) concentration and plasma for the determination of plasma MDA level were obtained. Using immunoassay methods and Bio–Plex Multiplex Immunoassay, the levels of melatonin and 25(OH)–vitamin D, osteopontin, omentin–1, adipsin, adiponectin, C–peptide, ghrelin, glucose–dependent insulinotropic peptide (GIP), glucagon–like peptide–1 (GLP–1), glucagon, insulin, leptin, plasminogen activator inhibitor–1 (PAI–1), resistin, and visfatin were determined in the serum. The results obtained from the laboratory tests were statistically analyzed. Differences at the level of $p < 0.05$ were considered statistically significant.

The foundation of the doctoral dissertation consists of three publications. Publication I (a review) describes the role of melatonin and vitamin D as antioxidants reducing the negative effects of exposure to ionizing radiation, used in cancer diagnosis and therapy.

Publication II (an original article) is a description of a study involving 45 patients diagnosed with HNC and 25 healthy people as a control group (CG, 55.36 ± 1.17 yrs). HNC patients were divided into two age groups: the younger cancer group (YCG, $n = 25$; 58.24 ± 1.29 yrs) and the older cancer group (OCG, $n = 20$; 69.7 ± 1.49 yrs). SOD–1 activity was similar in all analyzed groups. In contrast, CAT activity was statistically lower in both HNC groups (YCG and OCG) compared to CG. GPx activity was significantly higher in YCG compared to CG. There were no statistically significant differences in the concentration of MDA in erythrocytes between the study groups, but the concentration of MDA in plasma was significantly higher in patients with YCG and OCG than in CG. In OCG, the concentration of melatonin was significantly lower than in CG. The concentration of 25(OH)–vitamin D in the serum of healthy subjects was higher than in patients with YCG and OCG. In both groups of patients, the concentration of osteopontin was significantly higher than in CG.

The study described in Publication III (an original article) involved 46 patients with HNC and 23 healthy people as a control group (CG). HNC patients were divided into two subgroups of 23 people each based on their BMI, namely the normal BMI (nBMI; BMI < 25 kg/m^2) and the increased BMI (iBMI; BMI ≥ 25 kg/m^2). Patients in the nBMI group had significantly higher concentrations of adiponectin, omentin–1, and ghrelin in serum compared to iBMI. Significantly higher levels of insulin, leptin, C–peptide, GLP–1, PAI–1, resistin, and visfatin were observed in iBMI than in nBMI. There were no statistically significant differences between the nBMI and iBMI groups with regard to adipsin, GIP, and glucagon. Significantly higher levels of adipsin, visfatin, glucagon, and PAI–1, as well as a significantly lower level of ghrelin were found in nBMI compared to CG. The analysis showed no differences in the concentration of omentin–1, GIP, adiponectin, C–peptide, GLP–1, insulin, leptin, and resistin between nBMI and CG.

The results described in Publication II may indicate a redox imbalance in people with HNC. Higher plasma concentrations of MDA in the HNC patients indicate increased lipid peroxidation, which may be associated with carcinogenesis. In addition, lower levels of melatonin and 25(OH)–vitamin D and higher levels of osteopontin were observed in HNC patients, which may affect the development and course of the disease. Differences in the results between the younger and older groups of HNC patients indicate the need to take into account the age of patients in treatment strategies. In the study described in Publication III, significant differences in the concentrations of adipokines and factors regulating glucose metabolism were observed between HNC patients with different BMI and a healthy control group. These results suggest that obesity may influence metabolic processes and hormones involved in body mass regulation, which in turn may affect the development and course of HNC. Differences in biomarker concentrations between the nBMI, iBMI, and control groups indicate possible relationships between hormonal disorders and the pathogenesis of HNC.

Keywords: adipokines; antioxidants; carbohydrate metabolism; head and neck cancer; inflammation; lipid peroxidation; obesity; oxidative stress