14 STRESZCZENIE W JĘZYKU ANGIELSKIM/ SUMMARY

Cardiometabolic disorders and cardiovascular disease (CVD) are an increasing health challenge worldwide due to their steadily increasing prevalence, especially among women. For this reason, new biomarkers are still being searched for, which would facilitate faster and more accurate identification of people at increased risk of developing the disease, make it possible to monitor the level of individual metabolic risk, and which may be of potential therapeutic importance.

The main aim of this study was to assess the relationship between the concentration of branched-chain amino acids (BCAAs), tryptophan, selected tryptophan metabolites, and recognized cardiometabolic risk factors among women with normoglycemia and dysglycemia, including type 2 diabetes.

This dissertation consists of four scientific papers. The purpose of the first two papers (available as review articles), was to analyze and discuss, based on current knowledge, the role of selected amino acids, including branched-chain and aromatic amino acids, e.g. tryptophan, in metabolic disorders such as obesity, insulin resistance, and type 2 diabetes, leading to the development of cardiovascular diseases.

The aim of the first of the two original papers was to present the relationship between the total concentration of branched-chain amino acids (BCAA) in the blood serum and cardiometabolic risk factors in a group of 349 women aged 40 to 60 divided into two subgroups depending on the glycemic status: the group with normoglycemia (NG, n = 184) and the dysglycemic group (DG, n = 165). The concentration of total BCAAs (sum of L-leucine, L-isoleucine and L-valine) and total calcium (TCa) was determined. Fatty Liver Index (FLI) and albumin-corrected calcium (CCa) were calculated.

In both original papers, biochemical parameters such as triglycerides (TG), HDL cholesterol (HDL-C), creatinine, C-reactive protein (CRP), alanine aminotransferase (ALT), gamma-glutamyltransferase (GGT), insulin, thyroid stimulating hormone (TSH), glucose, glycated hemoglobin (HbA1c) were also determined in blood samples. HOMA-IR and eGFR were calculated. The systolic and diastolic blood pressures were measured twice and the body mass index (BMI) was calculated.

It was observed that serum total BCAA concentrations were significantly higher in the group of women with dysglycaemia (p<0.0001). Logistic regression analysis, adjusted for age and BMI showed that an increase in BCAA concentrations by 10 µmol/L significantly increased the chance of occurrence of concentrations above the 75th percentile for TCa, CCa and HbA1c, and HDL-C concentrations below 45 mg/dL in the DG group. Similar significant relationships were not observed in the NG group. Based on the obtained results, it was concluded that the state of dysglycemia predisposes women to significantly relationships between the total concentrations of BCAA and the level of calcium, HbA1c and selected lipid parameters, regardless of BMI and age. The relationships shown may reflect the potential mechanisms linking BCAAs with metabolic disorders, depending on the concentration of calcium.

The aim of the second original paper was to assess the relationship between tryptophan and its metabolites from the kynurenine pathway (KP), and the occurrence of type 2 diabetes and cardiometabolic risk factors in a group of 128 obese women aged 41 to 60 divided into two groups: a group with normoglycemia (NG, n = 65) and the group with type 2 diabetes (T2D, n = 65) = 63). Tryptophan (Trp), kynurenine (Kyn), 3-hydroxykynurenine (3-HKyn), kynurenine (Kyna) and quinolinic acid (QA) concentrations were determined in the serum. Following ratios were calculated: Kyn/Trp (KTR), Kyna/Kyn (KAT), 3HKyn/Kyn (KMO), Kyna/3HKyn and Kyna/QA. Significantly higher values of Trp, Kyna, Kyna/QA and Kyna/3HKyn were observed in the group of obese women with concomitant type 2 diabetes, compared to the group of obese women with normoglycaemia. Logistic regression analysis showed that Trp and Kyna concentrations and Kyna/3HKyn ratio values were mainly related to the occurrence of T2D, even after adjusting for confounding factors. The regression model with Trp and Kyna/3HKyn ratio as independent variables explained 20% of the variance of T2D incidence. Based on the obtained results, it was concluded that the increase in Trp and Kyna concentrations, along with the accompanying increase in the value of the Kyna/3HKyn index, is associated with the occurrence of type 2 diabetes among middle-aged obese women.

The presented results from both original and review papers indicate the significant role of branched and aromatic amino acids and their metabolites in cardiometabolic disorders among middle-aged women, which may be of therapeutic and diagnostic importance.