9. SUMMARY

Diseases of the cardiovascular system constitute a group of illnesses of the organs and tissues constituting the circulatory system, including ischemic heart disease, ischemic stroke, dyslipidemia, atherosclerosis and hypertension. This group of diseases have been identified as a pandemic of the 21st century and constitute the main cause of morbidity, disability and mortality in developed countries. The most important, independent risk factors of cardiovascular diseases include visceral obesity and accompanying chronic inflammation, disorders of lipid metabolism, diabetes and hypertension. A significant part of risk factors of cardiovascular disease results from improper lifestyle, including nutrition. Different proportions of macronutrients in the food intake may modify the metabolic and hormonal response of the body during the post-prandial period, and thus affect the cardiovascular risk. In addition, there are differences in post-prandial metabolic and hormonal response as well as energy expenditure and oxidation of macronutrients in people with different nutritional status.

The aim of the study is to evaluate the differences in the concentrations of selected metabolic, hormonal and pro-inflammatory risk factors of cardiovascular disease (glucose, insulin, triglycerides, homocysteine, leptin, adiponectin and TNF-α), as well as differences in energy expenditure, glucose and lipid oxidation between group of men with normal body mass, and a group of overweight/obese men after eating a high carbohydrate meal and after eating a high fat meal. Another aim of the study is a comparative analysis of the listed risk factors of cardiovascular diseases in the crossover study (after a high carbohydrate meal followed by a high fat meal) in the group of men with normal body weight and in the overweight/obese men group.

The work was carried out as part of the research project of the Ministry of Science and Higher Education: "Analysis of the genetic determinants of metabolic response to a diet with various carbohydrate, protein and fat contents. Searching for genetic markers for the individualization of nutrition of patients with obesity and type 2 diabetes" carried out at the Department of Endocrinology, Diabetology and Internal Diseases of the University Teaching Hospital in Bialystok in 2009-2015. The approval of the Bioethics Committee of the Medical University of Bialystok, no. R-I-002/35/2009. The study covered only men, in order to ensure the condition of homogeneity of the group (the aim of the study was not to analyze sexual dimorphism, which may be conditioned by the concentrations of selected factors). To the first

stage of the study, 475 men were qualified, in whom an oral glucose load test was performed on the first visit in order to exclude people with impaired carbohydrate metabolism from subsequent stages of the study. On the second visit, after exclusion from the study 164 men diagnosed with carbohydrate metabolism disorders, in the group of remaining 311 healthy men anthropometric measurements were made (height, body weight and BMI). Men with normal body mass (BMI < 25.0 kg/m² - group N) were qualified to the control group, whereas men with overweight/obesity (BMI ≥ 25.0 kg/m² - O/O group) were qualified to the study group. To participate in the next stages of the crossover study (visit III and IV) with the use of standardized isocaloric (450 kcal) Nutricia meals, only 43 men agreed to commit themselves to the not changes in the diet and the level of daily physical activity throughout the observation period. At the III visit cannons were inserted into the debridement vein for the examined men, and blood was collected on an empty stomach for the determination of concentration of glucose, insulin, triglycerides, leptin, adiponectin, homocysteine and TNF-α. Then, after a 30-minute resting in recumbence, the resting metabolism and oxidation of lipids and glucose by indirect calorimetry was evaluated. In the next part of visit III, for the examined men a high-carbohydrate meal was served (HC) Nutridrink Fat Free, in which 89% of energy comes from carbohydrates, 0% from fats and 11% from proteins. During 30, 60, 120, 180 and 240 minutes after the meal, venous blood was collected to determine the concentrations of all the above-mentioned biochemical parameters. The collected material was suitably protected and then prepared for markings in accordance with the manufacturer's instructions. Additionally, during 60, 120, 180 and 240 minutes after eating a meal, the energy expenditure, the lipid and glucose oxidation was determined. At an interval of 1-2 weeks from visit III, the examined men were referred back to the research center in the morning. Only 31 qualified men applied for IV visit. The resignation of 12 people was caused by the long duration of the study with the use of a standardized meal at visit III. Visit IV, on which the examined men consumed a high-fat meal (HF) Calogen (4% energy from carbohydrates, 96% from fats and 0% from proteins) proceeded according to the scheme of visit III. Finally, all the planned biochemical parameters as well as results from the measurement of energy expenditure, glucose and lipid oxidation, which were subjected to statistical analysis, were obtained only in 26 study participants (13 men with normal body mass and 13 men with overweight or obesity).

Our study showed that fasting glucose and after ingestion of both tested meals did not differ significantly between the group of men with normal body weight and men with

overweight/obesity (without any disturbed carbohydrate metabolism). In contrast, significantly higher concentrations of insulin were observed on an empty stomach and after a high-carbohydrate or high-fat meal intake in the overweight/obese group compared to the group with normal body weight.

According to the predictions of the crossover study, in both groups, significantly higher glucose and insulin levels were observed after a high-carbohydrate meal with compared to a high-fat meal. After a high-carbohydrate meal, in the final part of follow-up (240 minutes of the study) hypoglycemia episodes were found in 27% of all study participants. There were no significant differences in the HOMA-IR insulin resistance between the groups, however, in overweight/obese men, HOMA-IR was above the values considered to be normal. In addition to higher insulin concentrations in the group of overweight/obese men, significantly higher concentrations of fasting triglycerides and homocysteine were observed as well as after the intake of both meal (high-fat and high-carbohydrate) than in men with normal body mass. In the crossover study in both groups, higher concentrations of triglycerides and homocysteine were found after serving a high-fat meal in compared to a high-carbohydrate meal.

Analysis of cardiovascular risk factors resulting from secretory adipose tissue activity in men with overweight/obesity showed significantly higher levels of fasting leptin and during the entire observation, both after eating a high-carbohydrate meal and high-fat meal in compared to normal weight men.

In the crossover study, in the group of men with normal body mass a tendency to higher area under the curve of leptin concentration after a high-carbohydrate meal than high-fat meal was observed, which was not observed in people with overweight/obesity. The nutritional status of the men did not differentiate between adiponectin levels in fasting and post-prandial periods. In the crossover study, in the group of overweight/obese men, a significantly higher area under the adiponectin concentration curve after a high-fat meal with compared to the high-carbohydrate meal was observed, which was not noted in the group of men with normal body mass. Also, no significant differences were observed in fasting TNF-α concentrations as well as after eating a high-carbohydrate and high-fat meal between the study groups. However, in the crossover study in the overweight/obese group, there was a tendency to a higher area under the TNF-α concentration curve after a high-fat meal vs. a high-carbohydrate meal.

In the present study, energy expenditure and oxidation of energy substrates after consumption of isocaloric meals of various nutrient composition were also examined. There were no significant differences between the groups in resting metabolism and energy expenditure after both meals (high-carbohydrate meal and a high-fat meal). In the crossover study only in the group of overweight/obese men there was a significantly higher area under the curve of energy expenditure after a high-carbohydrate meal with compared to a high-fat meal. Higher oxidation of fasting lipids in the group of overweight/obese men was also shown compared to the men with normal body mass, which was not observed in relation to glucose oxidation. In the post-prandial period, an unfavorable, slower and later glucose oxidation after a high-carbohydrate meal was found, and lipids after a high-fat meal in overweight/obese males with normal body weight, which could indicate reduced metabolic flexibility in people with excessive body weight.

In summary, the study showed differences in the metabolic and hormonal response to food intake with different levels of macronutrients between men with different nutritional status. In the group of overweight/obese men, higher concentrations of fasting and post-prandial periods of insulin, triglycerides, homocysteine and leptin were observed compared to men with normal body mass. Also, a significant effect of the type of consumed meal on the metabolic, hormonal and proinflammatory response was demonstrated. After a high-carbohydrate meal, significantly higher glucose and insulin levels were found in both groups and a tendency to higher area under the curve of leptin concentrations in the group of men with normal body mass. However, after a high-fat meal in both groups, significantly higher concentrations of triglycerides and homocysteine were observed, and in the group of overweight/obese men significantly higher cardioprotective secretion of adiponectin (area under the curve) and a tendency for lower secretion of proinflammatory TNF-α.

Based on the conducted studies, it has been shown that people with overweight/obesity have an increased cardiometabolic risk, which results from the accumulation of assessed cardiovascular risk factors in them, both after serving a high-carbohydrate meal as well as a high-fat content. However, it seems that in the case of overweight/obese men, a slightly lower number of harmful effects caused a high-fat meal.