**Streszczenie w języku angielskim**

The aging population and medicine advancement contributes to the increasing number of people suffering from chronic kidney disease (CKD). Additional, presence of other civilization diseases, including cardiovascular disease (CVD) accelerates the progression of kidney failure and the onset of complications, including death. Symptoms and signs accompanying the CKD development appear already at the stage of advanced kidney damage. Appropriate prophylaxis, lifestyle modification, reduction of risk factors and targeted pharmacotherapy may slow down the development of further impairment of renal function. It is also important to remember about proper control of other diseases. For this reason, it is so important to search for new biomarkers that will enable appropriate prevention at an early stage of kidney disease.

In the late twentieth century, a new polypeptide was developed, named adrenomedullin (ADM). It is a protein with pleiotropic functions throughout the body. It exhibits vasodilatory, natiuretic and diuretic properties, which together have a hypotensive effect, but also regulates metabolic homeostasis, has antimicrobial properties, and affects cell proliferation and differentiation. The peptide is present in most tissues and its significant synthesis takes place in the endothelium of blood vessels. Unfortunately, due to its instability, short half-life, and binding to the H-binding protein, the detection of ADM is difficult. However, in parallel, in the process of ADM synthesis, there is formed a more stable sequence - mid-regional proadrenomedullin (MR-proADM). Additionally, it was confirmed that both peptides are produced from the precursor in equimolar amounts, which enables the use of immunoassays for MR-proADM to reflect the ADM blood concentration. The studies showed a higher concentration of the pro-adrenomedullin mid-region in numerous cardiovascular disorders, additionally, its prognostic role in infections and sepsis was determined. So far, there have been few studies evaluating the role of MR-proADM as a biomarker of CKD progression and concomitant cardiac burden.

The aim of the study carried out as part of this doctoral dissertation was to assess the concentration of MR-proADM in patients with chronic kidney disease and arterial hypertension, and to determine the relationship of it with the stage of CKD, the presence of hypertension and the coexistence of other cardiovascular complications. Additionally, an analysis of the N-terminal B-type natriuretic propeptide (NT-proBNP), a biomarker commonly used in daily clinical practice was performed.

Material and methods: The study included 160 patients admitted to the Second Department of Nephrology and Hypertension with Dialysis Unit, Medical University of Bialystok, Poland in 2017-2019 with stable chronic kidney diseases treated conservatively, with or without hypertension and a control group of 27 healthy volunteers, different in terms of sex and age, not suffering from chronic kidney disease, hypertension and cardiovascular diseases. The concentration of MR-proADM and NT-proBNP was determined in the serum of the study and control group using the ELISA method, and the above-mentioned parameters were analyzed, considering the information obtained from past medical history, an interview, physical examination, laboratory tests, blood pressure measurement and pharmacotherapy.

Results: MR-proADM level was significantly higher in serum of patients with CKD compared to the control group ($p < 0.0001$). However, the median protein concentration in the subsequent CKD stages did not differ statistically. Further analysis showed significantly higher levels of MR-proADM in the serum of patients in the initial stages of CKD (G1 and G2) than in the control group ($p < 0.05$). Comparing the relationship between MR-proADM concentration and echocardiographic parameters positive correlation was demonstrated with the increased left ventricular dimension ($p = 0.009$). Additionally, a positive correlation was found between the peptide concentration and the glucose concentration ($p = 0.017$). Among other laboratory parameters, a negative correlation was observed with iron concentration ($p = 0.03$). There was no significant correlation between the concentration of MR-proADM and the control of hypertension, other results of laboratory tests and pharmacotherapy. Patients with chronic kidney disease had higher level of NT-proBNP in the serum compared to the control group ($p < 0.0001$). In subsequent stages of CKD advancement, a further gradual increase in the median concentration was observed, which was associated with a higher range of peptide concentrations. Additionally, the serum concentration of NT-proBNP correlated with a positive history of heart failure, ischemic heart disease and echocardiographic cardiac dysfunction ($p < 0.05$). Then, an analysis of the correlation between the peptide concentration and the results of laboratory tests was performed. There was a significant positive correlation between serum NT-proBNP concentration and higher level of creatinine ($p < 0.0001$) and uric acid ($p < 0.05$), and a negative correlation with eGFR ($p < 0.0001$). Among the drugs used, the serum concentration of NT-proBNP was statistically higher in patients not using the ARB ($p = 0.002082$).

Conclusions: Patients with chronic kidney disease were characterized by significantly higher levels of MR-proADM when compared to healthy volunteers. The described relationship

may be used in the following years to identify patients among the general population. A parallel significant relationship between the concentration of MR-proADM and the early stages of CKD suggests the possibility of using the peptide as a biomarker of the development of kidney injury. The obtained data may indicate that the slightly impaired kidney function causes increased secretion of the peptide and MR-proADM plays a nephroprotective role. In the conducted study, unlike in other publications available in the literature, no significant difference in the concentration of MR-proADM was found in the subsequent stages of CKD advancement. This lack of correlation may be related to the uneven distribution of patients at different stages of CKD. Further statistical analysis showed a positive relationship between the higher concentration of MR-proADM and the presence of left ventricular hypertrophy, which can be used as a marker in screening. Additionally, it may indirectly indicate an increased cardiovascular risk in the group with risk factors. The lack of correlation with arterial hypertension may, in turn, be related to the pharmacotherapy or the presence of comorbidities. Regarding NT-proBNP an increase the protein's concentration in the study group was demonstrated as well as a further increase in the subsequent stages of CKD. Additionally, the obtained analyzes show a significant correlation between NT-proBNP and the parameters of kidney injury. The obtained results and previous reports, which described a persistently elevated protein concentration in patients with chronic kidney disease, suggest a limited usefulness of the protein in the assessment of the progression of kidney disease. The parallel reported significant correlation of NT-proBNP concentration with concomitant cardiovascular diseases and visualized cardiac dysfunction in echocardiography may mainly indicate the progression of heart disease in patients with CKD.

The results presented in the doctor's dissertation, although not always consistent with the data from previous studies, constitute a significant contribution to the evaluation of the use of MR-proADM as a biomarker for the assessment of CKD progression and the occurrence of cardiovascular complications at an early stage of its development. However, further studies are required to confirm the predictive role of the protein or to determine the use of MR-proADM as a therapeutic agent.