Rozdział 7. Streszczenie w języku angielskim

Hypertension is the most significant modifiable risk factor for cardiovascular diseases and the leading cause of premature death worldwide. Undoubtedly, on a global and widespread scale, it is considered a civilization disease. Understanding the multifactorial etiology of hypertension and the mechanisms of interaction of vasoactive regulatory mediators is crucial in establishing appropriate and effective treatment. Arterial hypertension is an insidious disease which, due to its latent, asymptomatic nature, may remain undiagnosed for a long time and lead to serious organ complications. Unfortunately, the etiology of this condition is so complex that its prevention mainly focuses on symptomatic treatment, lowering blood pressure, and treating complications. In 90% of cases, hypertension is primary of unknown cause, in the remaining cases, hypertension is secondary, related to other diseases and body dysfunctions.

One of the most severe organ complications of hypertension affects the heart. Chronic high blood pressure leads to perfusion disturbances, ischemia, and compensatory structural changes in this organ. As a result of tissue reconstruction and cardiomyocyte remodeling, systolic dysfunction, cardiac arrhythmias and in advanced stages, heart failure occurs. This leads to further consequences in the form of dysfunction of other organs due to insufficient tissue oxygenation.

Many factors and molecular pathways are involved in the regulation of blood pressure. Disruptions in their interactions and the balance of vasoconstrictive and vasodilatory factors, favoring the former, contribute to the pathogenesis of hypertension. Signal transmission pathways between cells are involved in all processes occurring in the body. The Wnt/β-catenin pathway participates in a wide spectrum of processes, including the proper development and differentiation of cells, such as cardiomyocytes. At the same time, disturbances in this signaling pathway are observed in the case of myocardial remodeling and fibrosis, which contribute to heart failure.

Considering the multifactorial etiology of hypertension and the lack of reports on the role of the Wnt/β-catenin pathway in this condition, the current study evaluated the immunohistochemical, morphometric, and gene expression profiles of Fzd8, Wnt1, GSK-3β, and β-catenin in the hearts of rats with primary and secondary hypertension.

The study was conducted on hearts collected from 24 male rats: 7 with primary hypertension (SHR) and 5 normotensive control animals (WKY), 7 with induced secondary hypertension (DOCA-salt), and 5 normotensive control rats post-unilateral

nephrectomy (UNX). After fixation in buffered formalin, the material was routinely processed into paraffin blocks. For the immunodetection of Fzd8, Wnt1, GSK-3β, and β-catenin, reactions were performed using antibodies against the studied proteins. The results of above reactions were assessed under a microscope connected to a computer equipped with Nikon's NIS-Elements Advanced Research software. Real-time PCR was used to compare the expression profile of *FZD8, WNT1, GSK-3β* and *CTNNB1* genes in the hearts of control and hypertensive rats. The reference gene was the GAPDH gene.

The obtained data were subjected to statistical analysis using the STATISTICA 13.3 software package. For measurable features, the arithmetic mean and standard error (SE) were calculated. Statistical analysis was performed using one-way ANOVA. Fisher's test was used for post-hoc analysis, with a significance level of $p<0.05$.

Observation and densitometric analysis showed a decrease in the intensity of the immunohistochemical reaction for Fzd8, Wnt1, GSK-3β and β-catenin in the hearts of rats with essential hypertension (SHR) and an increase in these parameters in cardiomyocytes of rats with secondary hypertension (DOCA-salt) compared to normotensive animals WKY and UNX.

PCR results demonstrated a decrease in the expression of *FZD8, WNT1, GSK-3β,* and *CTNNB1* genes in the hearts of SHR animals compared to controls, particularly significant for *WNT1* and *CTNNB1*. However, an increase in the expression of these genes, statistically significant for *WNT1* and *CTNNB1*, was observed in DOCA-salt rats, compared to normotensive UNX rats.

The obtained results revealed changes in immunoreactivity and expression of genes encoding Fzd8, Wnt1, GSK-3β, and β-catenin in the hearts of rats with primary and secondary arterial hypertension. The decrease in the activity of Wnt/β-catenin pathway in the hearts of rats with essential hypertension and its increase in secondary hypertension suggest a different type of involvement of this signaling pathway depending on the etiology of hypertension. These results may contribute to a better understanding of the etiology of hypertension and constitute a basis for further research on this condition.