1. Streszczenie w języku angielskim

Metabolic dysfunction-associated steatotic liver disease (MASLD) is one of the most common complications of obesity. Its early stages are frequently asymptomatic, making diagnosis challenging. Established diagnostic techniques—such as liver biopsy, ultrasonography, dynamic pulse elastography, computed tomography, and magnetic resonance imaging – are not typically available for routine screening. Considering the significant role of both visceral (VAT) and total adipose tissue in the development of MASLD, quantifying adipose tissue content and distribution using bioelectrical impedance analysis (BIA) could serve as a useful tool for identifying individuals at elevated risk. Additionally, evaluating systemic inflammation and the levels of specific adipokines and cytokines may aid in diagnosing metabolic disorders associated with obesity and MASLD.

This doctoral dissertation comprises three publications. The first is a review article that summarizes the current state of knowledge regarding the role of selected adipokines and cytokines in the pathogenesis of obesity. A comprehensive analysis of the scientific literature and existing studies suggested that certain adipokines and cytokines might hold diagnostic potential for obesity, and it highlighted the possibility of using saliva as a biological matrix for assessing these markers. Moreover, the review identified a relatively unexplored area – assessing the diagnostic utility of these markers in both serum and saliva in the context of MASLD. These findings provided the research foundation, which aimed to evaluate the relationship between adipose tissue content/distribution and hepatic steatosis development, as well as to examine correlations between selected adipokines and cytokines in serum and saliva among individuals with MASLD.

The study received ethical approval from the MUB Bioethics Committee. Participants included men and women aged 20–55 years with primary obesity (first and second degree) as well as individuals with normal weight. Subjects underwent standard anthropometric measurements and body composition analysis via BIA, with waist fat area assessed accordingly. Liver stiffness and steatosis were measured using dynamic pulse elastography (VCTE). Venous blood samples were collected from all participants. The serum was used for biochemical parameters concentration analysis. Furthermore, it has been used to determine concentrations of adiponectin, resistin, tumor necrosis factor α (TNF-α), interleukin 6 (IL-6), interleukin 1β (IL-1β), interleukin 23 (IL-23), extracellular matrix metalloproteinases MMP-2

and MMP-9. Saliva samples were also collected to determine the levels of resistin, visfatin, TNF-α, IL-6, IL-1β, MMP-2, and MMP-9. Data were analyzed using Statistica 13.3 software.

The second research study in this series of publications evaluated selected pro-inflammatory adipokines and cytokines in unstimulated saliva from patients with obesity and hepatic steatosis at varying stages (with minimal or no fibrosis), assessing these parameters for their potential as early markers of NAFLD/MASLD. Participants were divided into five groups based on body mass index (BMI) and the presence and severity of hepatic steatosis. Statistically significant differences emerged between the groups regarding the median salivary concentrations of IL-1β and resistin. Moreover, salivary levels of IL-1β, resistin, and MMP-2 were found to increase significantly with the progression of hepatic steatosis, as evaluated by the CAP parameter.

The subsequent study aimed to evaluate and compare serum adipokine and cytokine concentrations in normal-weight and obese subjects differentiated by MASLD, while also assessing the potential diagnostic utility of these parameters. In addition, the study sought to establish a cutoff value for body fat content associated with an increased risk of developing hepatic steatosis. Participants were categorized into three groups according to BMI and the presence of MASLD. Using a combination of 12 multiple regression models, it was observed that in women, a higher degree of hepatic steatosis was significantly associated with increased percent body fat, a larger VAT area, elevated VAT/SAT and HOMA-IR ratios, as well as higher levels of IL-6 and IL-1β. In men, a significant association was found between more severe liver steatosis and increased percent body fat, a larger VAT area, and higher IL-6 concentrations. Cutoff points for adipose tissue parameters determined to indicate an increased likelihood of developing liver steatosis were also established.

Multivariate analysis demonstrated a significant association between the development of hepatic steatosis and both total body fat and the visceral adipose tissue area (measured by BIA). The diagnostic value of assessing the visceral adipose tissue area (using defined cutoff points) for evaluating the risk of developing MASLD in both sexes was confirmed. Among the adipokines and serum cytokines examined, interleukin 6 emerged as the strongest predictor of MASLD in both men and women, while interleukin 1β was predictive only in women. Analysis of the results further indicated that among the adipokines and cytokines assessed in saliva, only IL-1β, MMP-2, and resistin correlated significantly with the presence of MASLD; however, these findings require confirmation in a larger cohort. Overall, the results emphasize the need for further studies involving larger populations with gender-

specific analyses and including the full spectrum of MASLD stages (from fatty liver disease to MASH and hepatic fibrosis) to identify adipokines and cytokines specific to each stage of the disease.