SUMMARY

Obesity is one of the most pressing issues the civilization faces in the 21st century, affecting millions of people worldwide. The condition develops primarily due to imbalance of caloric intake and energy spending, which results in accumulation of excess nutrients in tissues and subsequent weight gain. This abnormal increase in body fat is associated with numerous adverse health effects, among which are chronic low-grade inflammation, disturbances in insulin signalling and glucose homeostasis or ectopic lipid accumulation and lipotoxicity. The conditions comorbid with obesity include metabolic syndrome, type II diabetes, cardiovascular disease, breathing issues, cognitive impairments, and various types of cancer. When obesity of over 35 kg/m^2 BMI is accompanied by comorbidities, it is termed morbid obesity (MO) and should be treated. Bariatric surgery is the most effective method for sustained weight loss with a remarkable benefit of reversing the related adverse health effects e.g., remission of diabetes. Disturbed lipid metabolism is an intrinsic quality of MO. However, despite advances in analytical methods, many studies assessing the changes in lipidome frequently analyse only serum lipid profiles, missing the biologically relevant fatty acid (FA) disturbances. This dissertation intends to demonstrate how one anastomosis gastric bypass (OAGB), a relatively frequently performed but understudied in terms of its effects at the lipidome level bariatric surgery, affects the levels of FAs and in particular bioactive groups of FAs i.e., branched chain FAs (BCFAs), odd-chain FAs (OCFAs) and polyunsaturated FAs (PUFAs).

Total FA profiles were analysed with gas chromatography-mass spectrometry (GC-MS) in serum and adipose tissue of bariatric patients. At baseline patients presented with significantly lower levels of BCFA in serum and visceral adipose tissue and the OAGB treatment led to restoration of appropriate BCFA levels. Recent evidence of BCFA synthesis from branched chain amino acids (BCAA) precursors in human adipose tissue suggested possible involvement of this process in attenuated BCFA content with MO subjects. In collaboration with the Medical University of Gdansk, the analysis of serum BCAA concentrations and expression of enzymes catalysing their transformation was performed and results were in line with the initial hypothesis.

Analysis of circulating FAs at two time points after the surgery revealed profound changes that may be of clinical relevance. Two weeks after the surgery the levels of BCFAs, OCFAs and essential PUFAs were significantly lower. These results suggest that MO patients undergoing OAGB could benefit from interventions that improve levels of these FAs, be it in a form of supplementation or dietary adjustments, due to these FAs having effects aligning with the goals of bariatric treatment i.e., resolution of inflammation (PUFAs) and improved insulin sensitivity (BCFAs), lower cardiovascular risk (OCFAs). Principal component analysis (PCA) has shown that, unlike amino acids concentrations, which normalize in serum at 6-9 months after OAGB, profiles of FA remain altered at this point in time. Despite improvements in BCFA and OCFA content, reduced levels of some PUFAs persisted, although some identified changes may be beneficial e.g. low level of potent proinflammatory FA – arachidonic acid.

The subject of possible PUFA involvement in regulation of inflammation after OAGB was expanded with analysis of their downstream metabolites – oxylipins. To this end, tandem mass spectrometry coupled with liquid chromatography and sample preparation by solid phase extraction (SPE-LC-MS/MS) method was developed. This allowed for successful quantification of the number of oxylipins in serum and enabled the detection of differences in their concentrations before and after OAGB surgery.

Finally, a mouse model of obesity was implemented to gain insight into FA alterations in heart and brain tissue, in order to shed some light on the possible role that FAs have in MO-associated cardiovascular risk and cognitive impairment respectively. SPE was employed during sample preparation in order to obtain separate fractions of polar lipids which are components of membranes and neutral lipids that mainly store energy. In the brain, eicosapentaenoic acid, FA involved in maintaining healthy brain function, was depleted. In turn, the disturbances of heart function were accompanied by PUFA accumulation in membrane lipids.

Results of presented studies provide valuable insight into changes in a biologically important group of metabolites, FAs, occurring in MO and after OAGB procedure. This not only allows for better understanding of physiological changes that come with understudied bariatric surgery but may also be of clinical relevance since many of identified changes concern essential and diet-derived FAs, which could be supplemented in order to facilitate bariatric treatment