An untargeted metabolomics approach to characterize short-term and long-term metabolic changes after bariatric surgery

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**ABSTRACT** Bariatric surgery is currently one of the most effective treatments for obesity and leads to significant weight reduction, improved cardiovascular risk factors and overall survival in treated patients. To date, most studies have focused on short-term effects of bariatric surgery on the metabolic profile and found that responses vary greatly among individuals. The aim of this study was to identify relevant metabolic changes not only shortly after bariatric surgery but also up to one year after the intervention. 132 serum samples taken from 44 patients from a clinical study before surgery, after hospital discharge (2-3 weeks after surgery) and at a 1 year follow-up were analyzed by using LC-HRMS (HILIC-QExactive). Raw data was processed with XCMS and normalized through quantile regression based on quality controls. 177 relevant metabolic features were selected through Random Forests and univariate testing and 36 metabolites of these metabolic features were identified including trimethylamine-N-oxide, alanine, phenylalanine and indoxyl-sulfate. Metabolic profiles followed different trend pattern over time which describe various metabolic effects of bariatric surgery. Our analysis highlights the importance of analyses at multiple points in time in subjects undergoing bariatric surgery to identify novel biomarkers for treatment response and cardiovascular benefit.

**Keywords**: obesity, LC-HRMS, gastric bypass, BCAA, TMAO, Random Forests, diabetes, drift-correction, metabolic changes, cardiovascular risk