An untargeted metabolomics approach highlights short-term and long-term effects of bariatric surgery in humans

Sophie H. Narath[1], *Eva Svehlikova*[2], *Bernd Schultes*[4], *Thomas R. Pieber*[1,2,3], *Frank M. Sinner*[1,2], *Edgar Gander*[1], *Harald Sourij*[2,3], *Christoph Magnes*[1]

CONTACT

1
JOANNEUM RESEARCH
Forschungsgesellschaft mbH

HEALTH
Institute for Biomedicine
and Health Sciences

Sophie H. Narath

Neue Stiftingtalstrasse 2
8010 Graz, Austria

Phone +43 316 876-41 00
Fax +43 316 8769-41 00

health@joanneum.at
www.joanneum.at/health

Medical University of Graz

2
Medical University of Graz
Division of
Endocrinology & Metabolism

Auenbruggerplatz 15
8036 Graz, Austria

CBmed BIOMARKER RESEARCH

3
CBmed
CENTER FOR BIOMARKER
RESEARCH IN MEDICINE

Stiftingtalstrasse 5
8010 Graz, Austria

eSwiss MEDICAL & SURGICAL CENTER

4
eSwiss
Medical and Surgical Center

9016 St. Gallen, Switzerland

Introduction

Bariatric surgery is currently considered one of the most effective treatments of obesity, leading to a recovery of the patient's metabolism. Besides the highly individual metabolic effects of bariatric surgery, the reduction of cardiovascular risks is an important aspect to be assessed. The aim of this study was to identify and quantify relevant metabolic changes which occur shortly after the surgery and after one year in a long term follow-up.

Methods

LC-HRMS (HILIC-QExactive) was used to analyze 132 serum samples from 44 patients before surgery (PRE), after hospital discharge (POST) and at a 1 year follow-up (FU). The raw data was processed with open source R package XCMS, optimized by IPO(1,2) and normalized through quantile regression based on quality controls.

Combining Random Forests and paired-t-tests defined a process to select metabolic features that describe the changes between two time points.
The same metabolic feature selection process was applied to compare time-point 1 and 2 (PRE-POST) as well as time-point 1 and 3 (PRE-FU).
The intersection of the selected characteristic metabolic features frowm both comparisons represents the combined information of short- and long-term effects of bariatric surgery.

Results

Metabolic feature selection resulted in 177 metabolic features that describe short-term and long-term effects and subsequently 36 metabolites were identified.

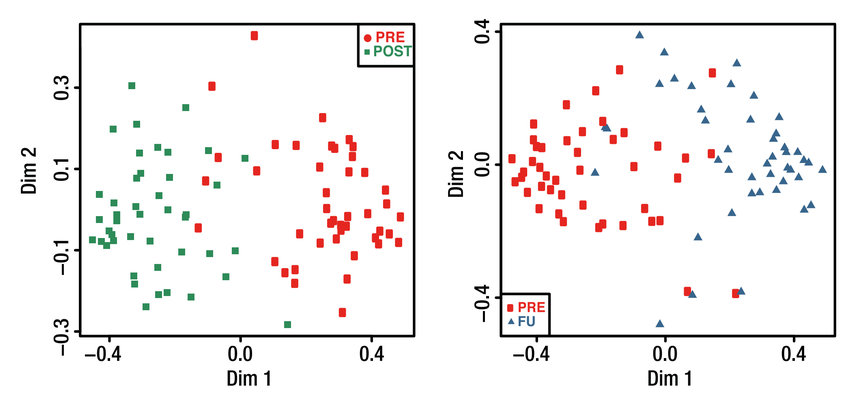

Figure 1: *Multi-Dimensional-Scaling showing distinct clustering of plots from supervised Random Forests, showing clustering for samples taken before and after the surgery for both time-points.*

8 metabolites were linked to cardiovascular risk: TMAO, indoxyl sulphate (increasing trend), choline, alanine, phenylalanin, tyrosine, valine, leucine/ isoleucine (decreasing trend).

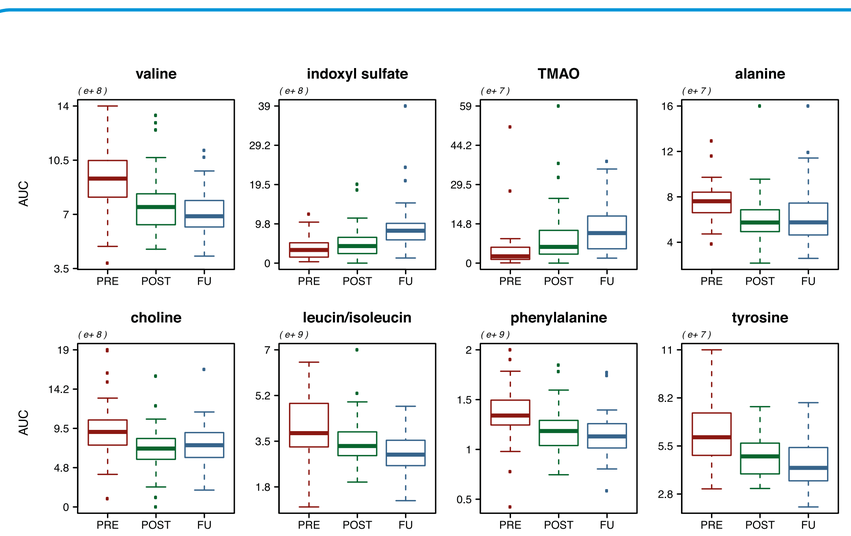

Figure 2: *Changes in the intensities (peak-AUC) of identified metabolites before and after bariatric surgery*

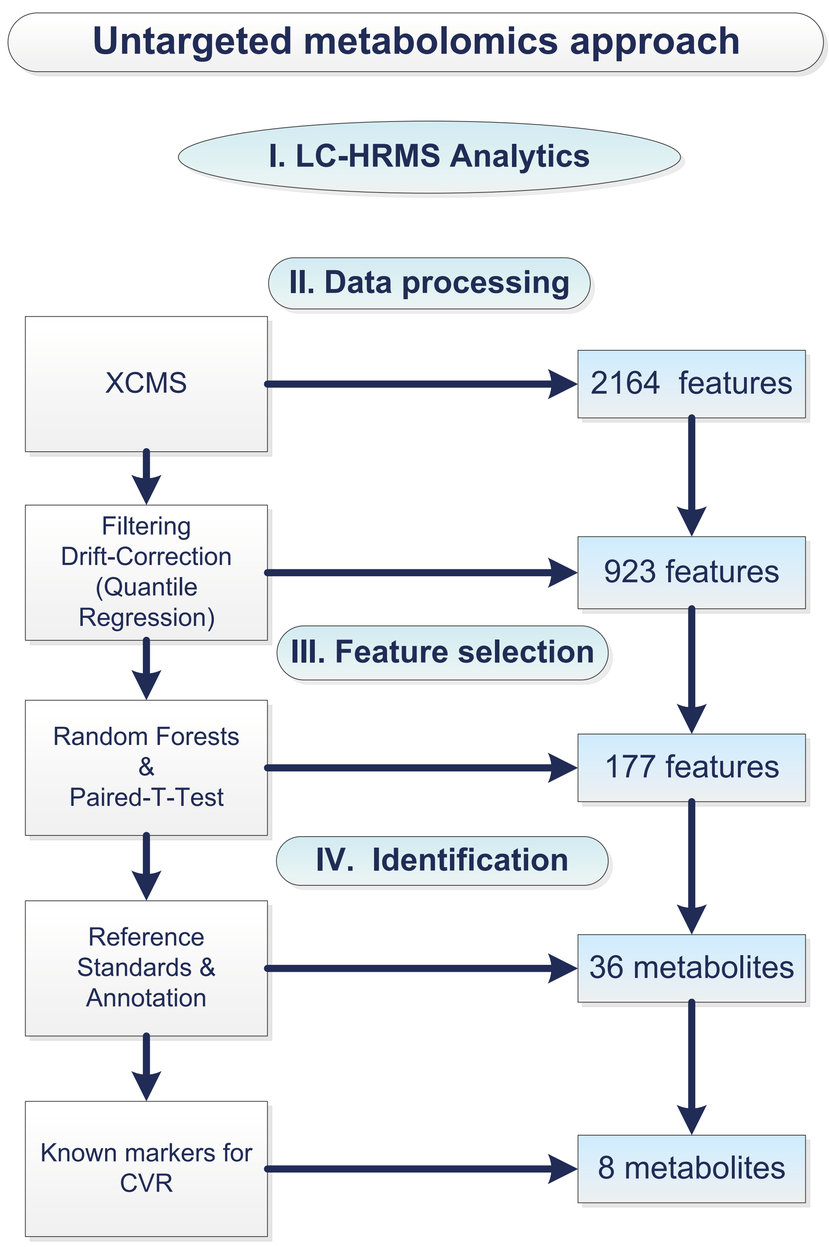

Figure 3: *Scheme of untargeted metabolomics approach (CVR=cardiovascular risk)*

Conclusion

The identified metabolites showed different trend-patterns over time, highlighting the importance of short and long-term metabolomics assessment after bariatric surgery. For the development of potential prognostic markers, metabolites with a negative or a positive median trend are better suited for further investigations rather than metabolites with an alternating zigzag course. This study links short-term and long-term metabolic changes after bariatric surgery by using an untargeted metabolomics approach.

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