**METABOLOMIC FOOTPRINT OF BARIATRIC SURGERY**

Jiun-Ruey Hu, MD, MPH1, Priya Umapathi, MD2, Gary Gerstenblith, MD2, Josef Coresh, MD, PhD3, Chiadi Ndumele, MD, PhD2,3

Author Affiliations:

1. Department of Medicine, Vanderbilt University Medical Center, Nashville, TN, 37212
2. Division of Cardiology, Department of Medicine, Johns Hopkins University, Baltimore MD, 21205
3. Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore MD, 21205

**BACKGROUND:** Morbid obesity, defined as body mass index (BMI) > 40 kg/m2, now affects 6.6% of Americans, and carries high cardiovascular risk. Bariatric surgery not only achieves significant weight loss but also induces metabolic changes that reduce cardiovascular risk, sometimes as profound as resolution of insulin resistance. The purpose of this study was to identify patterns in serum metabolites level alterations with bariatric surgery, to uncover metabolic pathways perturbed by bariatric surgery.

**METHODS:** We performed untargeted liquid chromatography with mass spectroscopy in fasting serum samples from 25 subjects in BARI-Heart, a prospective cohort study of morbidly obese adults undergoing bariatric surgery in Maryland from 2014-16. Participants provided serum samples at 3 visits: 2 pre-surgery and 1 post-surgery. We used a mixed effects model with random intercept to determine if the addition of visit number would significantly change a model that regressed metabolite levels only onto age and sex, as assessed by analysis of variance (ANOVA). Only metabolites that withstood Bonferroni correction for multiple comparisons were deemed significant.

**RESULTS:** Metabolomic profiling revealed 736 named non-drug metabolites. 90% of the variation in the metabolome could be explained by 31 principal components, with the top principal component explaining 39% of the variation. Mixed effects analysis identified 74 serum metabolites whose levels changed significantly with bariatric surgery. Thirty-six of these metabolites belonged to the lipid super-pathway. Fifty-one of the identified metabolites dropped in levels with surgery. Androstenediol (3β,17β) monosulfate was most significantly associated with change in weight.

**CONCLUSIONS:** Bariatric surgery is associated with significant changes in the levels of a multitude of serum metabolites. This represents, to the best of our knowledge, the largest metabolomic profiling effort in bariatric surgery patients to date.

**CONTENT CATEGORY:** EPIDEMIOLOGY

**KEYWORDS:** *obesity, metabolomics, bariatric surgery, lipids, cardiometabolic risk*