Impact of Roux-en-Y gastric bypass on metabolomic profile of obese women with type 2 diabetes

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Type 2 diabetes (T2D) remission rates reach up to 60% after Roux-en-Y gastric bypass (RYGB) in obese patients, but the precise mechanisms are not fully understood. We developed a prospective clinical study to investigate the molecular basis of these metabolic alterations through metabolomics. Plasma and urine samples were collected from 23 obese women with T2D before and after 3 months of RYGB. Subjects were analysed together and divided according T2D remission. Metabolomic profile exhibited a discriminatory pattern of alterations, suggesting important differences between patients with and without T2D remission. The main metabolites involved in these alterations includes bile acids, uremic toxins produced by microbiota, dicarboxylic acids, and different lipid classes. The contrast of the metabolite alterations allowed us to suggest several hypotheses. T2D remission could be associated with metabolic flexibility improvement, stimulated by increased oxidation and nuclear receptors activation, modifying lipid and glucose metabolism. In contrast, non-remission of T2D in obese patients after RYGB could be related to a subclinical kidney dysfunction. This was hypothesized considering that metabolic alterations observed on T2D remission rely on kidney function and its local enzymes and metabolite alterations of patients who do not present T2D remission could be associated to kidney disturbances. Thus, we suggest that RYGB deeply changes metabolomic profile and develop a functional role, including – but not limited to – regulation in the substrate flux and utilization, microbiota composition or activity and activation of nuclear receptors. These metabolic alterations seem to act together to form a circuit of alterations that activate triggers that lead to T2D improvement, which deserves future investigations.

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