Ranking factors involved in diabetes remission after bariatric surgery using machine-learning integrating clinical and genomic biomarkers

As weight-loss surgery is an effective treatment for the glycaemic control of type 2 diabetes in obese patients, yet not all patients benefit, it is valuable to find predictive factors for this diabetic remission. This will help elucidating possible mechanistic insights and form the basis for prioritising obese patients with dysregulated diabetes for surgery where diabetes remission is of interest. In this study, we combine both clinical and genomic factors using heuristic methods, informed by prior biological knowledge in order to rank factors that would have a role in predicting diabetes remission, and indeed in identifying patients who may have low likelihood in responding to bariatric surgery for improved glycaemic control. Genetic variants from the Illumina CardioMetaboChip were prioritised through single-association tests and then seeded a larger selection from protein–protein interaction networks. Artificial neural networks allowing nonlinear correlations were trained to discriminate patients with and without surgery-induced diabetes remission, and the importance of each clinical and genetic parameter was evaluated. The approach highlighted insulin treatment, baseline HbA1c levels, use of insulin-sensitising agents and baseline serum insulin levels, as the most informative variables with a decent internal validation performance (74% accuracy, area under the curve (AUC) 0.81). Adding information for the eight top-ranked single nucleotide polymorphisms (SNPs) significantly boosted classification performance to 84% accuracy (AUC 0.92). The eight SNPs mapped to eight genes — ABCA1, ARHGEF12, CTNNBL1, GLI3, PROK2, RYBP, SMUG1 and STXB5 — three of which are known to have a role in insulin secretion, insulin sensitivity or obesity, but have not been indicated for diabetes remission after bariatric surgery before.