Dia-Bar-Check: A new approach

Type-2-diabetes and bariatric surgery

The growing epidemic of obesity and its myriad medical (i.a. type 2 diabetes) and economic complications have highlighted the limitations of the available therapeutic options. Statistically, lifestyle modification remains the most effective public solution for obesity in general. However, for individual patients with severe or medically complicated obesity, bariatric surgery provides the greatest, most reliable, and most durable benefit.

Obesity, the accumulation of excess body fat, results from imbalances in the physiological mechanisms that regulate nutrient intake and assimilation, energy balance, and metabolic function. Dysfunction of these powerful regulatory systems, whatever the cause, has proven extremely difficult to fix, making the effectiveness of bariatric surgery that much more remarkable. Over the past several years, there has been a growing recognition of the highly beneficial effects of bariatric surgery on type 2 diabetes (T2D), with a large number of patients exhibiting what appears to be a complete remission of this disorder (Pories et al., 1995). Further strong evidence (Vidal et al., 2007; Mingrone et al., 2012; Sjöström et al., 2013; Schauer et al., 2016) now demonstrates that bariatric procedures markedly improve or cause remission of T2D, in part through weight-independent mechanisms, and that baseline BMI does not predict surgical benefits on glycemic or cardiovascular outcomes.

This impels consideration of such operations as “metabolic surgery,” which is used expressly to treat T2D, including among patients with a BMI <35 kg/m² who constitute the majority of people with diabetes worldwide. But not every patient show a remission of T2D after bariatric surgery (diabetes remission occurred in 42% up to 95 % of the patients undergoing bariatric surgery). Next to the question of the mode of action of metabolic surgery in a remission of T2D there is the unanswered question of which patient will profit from bariatric surgery with regard of a remission of T2D. Here the Dia-Bar-Check test could help by identifying these patients who have a subclinical inflammatory response or a cellular dysfunction in the adipose tissue, which is associated with T2D.

Bariatric surgery and the Dia-Bar-Check

The underlying mechanisms which leads to a remission of T2D after bariatric surgery is not known. It is assumed that weight loss-independent effects cause the change in endocrine, neural and endoluminal signal paths of the gastrointestinal tract. By altering these signaling pathways from the gut, these operations cause the body to seek a state of diminished fat storage and healthier metabolic function (Lee et al., 2012). In addition to the aforementioned changes in the gastrointestinal tract, a bariatric procedure also ensures that the subsequent food intake will be less than before surgery, next to a malabsorption of ingested calories and decrease of triglyceride levels. These changes improve the lipid and glucose metabolism and reduce inflammatory reactions in dysfunctional subcutaneous adipose tissue. Thus the burden of an unbalanced hyperplasia and/or hypertrophy in adipose tissue will contemporary be less and the metabolic function of adipose tissue will be restored to a balanced state.

Based on Lipozyt’s frozen test assay and Lipozyt’s statistical analysing mechanisms the Dia-Bar-Check enables to determine in advance whether an obese T2D-patient will respond

positively on bariatric surgery, i.e. improvement of diabetes or even T2D remission. The basic principle of the Dia-Bar-Check is to identify dysfunctional adipose tissue with regard to e.g. hyperplasia (too many immature preadipocytes), hypertrophy ("overcharged" adipocytes), dysfunctional adipokine production, and a state of chronic subclinical inflammation. Therefore, individuals with a dysfunctional adipose tissue will especially benefit from bariatric surgery in contrast to individuals with healthy and functional adipose tissue.

By measuring the activity of certain genes in adipose tissue aspirates with quantitative real-time PCR, the Dia-Bar-Check allocates individuals to a particular high-risk group by means of analysis with Kohonens self-organizing maps. Currently five high-risk groups are characterized and further groups could be refined. The five high-risk groups are characterized as follows: 1. non-diabetics, 2. diabetics with an immature adipose tissue (high fraction of immature preadipocytes (high *HMGA2* values), 3.diabetics with chronic subclinical inflammation (high *IL-6* values), 4. diabetics and "prediabetics" with a functional adipose tissue (high *PPAR-γ* and *ADIPOQ* values) and 5. further non-diabetics. Presumably, patients of groups 2 and 3 would benefit from bariatric surgery, because due to the restriction in food intake no new preadipocytes must be generated (high-risk group 2) and inflammation reactions diminish (high-risk group 3). This reduces the stress response in the adipose tissue and thus improves the functionality as well as the improvement/ a remission of the T2D. Patients in high-risk group 4 on the contrary would not benefit from bariatric surgery, because of a healthy and functional adipose tissue. The reason of T2D disease in this group should be sought in the area of insulin secretion in ß-cells of pancreas and impaired insulin sensitivity in muscle tissue or the liver.