

2 Disease Foundation and Management Challenges

2.1 Obesity with insulin resistance and chronic inflammation

Obesity is a key factor causing insulin resistance and chronic low-grade inflammation, and insulin resistance and chronic low-grade inflammation are key causes of type 2 diabetes (Zatterale et al., 2020; Ahmed et al., 2021). When there is an excessive accumulation of adipose tissue (especially visceral fat), metabolism becomes more active, and inflammatory factors such as TNF- α and IL-6 are continuously released. These substances can interfere with the signal transmission of insulin and fail to function in the human body.

Chronic inflammation related to obesity can affect multiple organ systems and is closely associated with the occurrence of cardiovascular diseases, non-alcoholic fatty liver disease and chronic kidney disease. These pathological changes superimpose on each other, continuously promoting blood sugar imbalance and increasing the risk of diabetic complications. It is suggested that during the treatment of diabetes, attention should be paid simultaneously to the regulation of body weight status and inflammation level (Zatterale et al., 2020; Kojta et al., 2020).

2.2 The effect of lifestyle intervention is limited

Adjusting diet and increasing physical activity are the main methods for diabetic obese patients to control their weight. These methods can help with weight loss and improve blood sugar in the short term, but many patients have difficulty adhering to them in the long term, and the actual effect is often underestimated (Kheniser et al., 2021; Meir et al., 2025). During the process of losing weight, the body will have automatic responses, such as reduced energy consumption and feeling hungry more easily, which leads to easy weight rebound and affects the long-term effect (Aronne et al., 2021; Petroni et al., 2021).

Research has found that few people can maintain their weight loss effect in the long term merely by changing their lifestyle. Most patients' weight will gradually rebound and approach the pre-intervention level after reaching a certain stage of weight loss (Petroni et al., 2021; Meir et al., 2025). Weight regulation is influenced by multiple factors, including the body's own regulation, psychological state and the surrounding environment, etc. A single lifestyle intervention cannot meet the complex long-term management needs, so drug treatment or metabolic surgery is often regarded as an important supplement.

2.3 Some traditional hypoglycemic drugs may cause weight gain

Some traditional hypoglycemic drugs, such as insulin and sulfonylurea drugs, although they can lower blood sugar, may cause weight gain during the medication process. This has led to some patients, although their blood sugar levels have improved, having more severe obesity problems and the difficulty of treatment has also increased accordingly. The GRADE study indicates that treatment regimens such as insulin glargine and glimepiride can better control blood sugar, but they also lead to more significant weight gain and increase the risk of hypoglycemia, cardiovascular and kidney diseases (Wexler et al., 2025).

This therapeutic dilemma suggests that hypoglycemic strategies need to take into account the overall metabolic benefits and emphasize individualized plans. New-generation hypoglycemic drugs such as GLP-1 receptor agonists and SGLT2 inhibitors have neutral or weight-reducing effects while controlling blood sugar, which are more in line with the treatment needs of patients with diabetes complicated with obesity. Therefore, they have gradually been included in relevant guidelines and are recommended as preferred plans.

3 Overview and Clinical Localization of Three Types of GLP-1 RAs

3.1 Insulin therapy based on enterotropin

glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are a class of hypoglycemic drugs whose main function is to regulate insulin secretion, and their mode of action is similar to the physiological effect of natural GLP-1 in the body after eating. When blood sugar levels rise, such drugs can promote insulin secretion and inhibit the release of glucagon, thereby helping to control blood sugar levels. Because its effect is glycemic-dependent, the risk of hypoglycemia is relatively low when used alone.