Remission of type 2 diabetes; Myths or Fact?

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Introduction:

The natural course of type 2 diabetes is described as a status of chronic progressive hyperglycemia, that may have started up to several years before diagnosis takes place. In most patients with type 2 diabetes, there is a progressive decline in the functions of β- cells, requiring further addition of anti-diabetic medications along the journey of diabetes. (1) Although type 2 diabetes is a multifactorial disease, genetic predisposition, in addition to lifestyle changes and weight gain play a critical role in the disease progression. (2) The concept of diabetes remission was introduced earlier when the normalization of glycemic profiles had been reported and maintained without intervention among some individuals. Several strategies were followed in a number of trials, including metabolic surgery, intensive therapeutic lifestyle changes, and some recent therapeutic interventions.

Thus, an expert consensus adopted the new concept of diabetes remission in 2009, which was further updated in 2021. (3, 4)

What is meant by type 2 diabetes remission?

Table (1) shows the definition of type 2 diabetes remission based on the consensus published by expert groups from USA and Europe. It is noteworthy to consider that this definition is based on expert opinion as the evidence is still needed for further understating of the durability of diabetes remission, and the long- term related consequences.

Table (1): Remission of type 2 diabetes mellitus as defined by the expert consensus in 2009 and updated in 2021. (3, 4)

Consensus in 2009	**Consensus update in 2021**
Partial remission: Hyperglycemia is less than the diagnostic thresholds for diabetes, lasting for at least 1 year, without any pharmacological treatment or ongoing intervention.	**Remission:** Is defined as the return of HbA1c below 6.5% for at least 3 months, either following an intervention or spontaneously.
Complete remission: Normal glycemic profile for at least 1 year, without any pharmacological treatment or ongoing intervention.	**Alternative criteria:** Fasting plasma glucose values less than 126 mg/dl Or estimated HbA1c less than 6.5% as calculated through continuous glucose monitoring measures.
Prolonged remission: At least 5 years duration of complete remission.	

Adapted from Buse et al. (3), and Riddle et al. (4), with the permission from Oxford University Press.

Applied strategies for Type 2 diabetes remission:

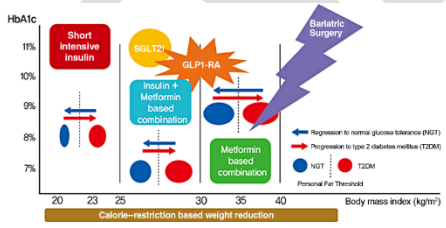
Although the concept of remission of type 2 diabetes is a recent concept, several reports show promising results.

Metabolic surgery for patients with type 2 diabetes and obesity:

Several randomized clinical studies confirmed the concept of diabetes remission following metabolic surgical intervention. There are several procedures for metabolic surgery which succeeded to promote significant weight loss, and improvement of the glycemic profile. However, Roux-en-Y gastric bypass (RYGB) surgery were two- fold likely to have diabetes remission compared to laparoscopic adjustable gastric banding (LAGB). (5) Metabolic surgery is an invasive procedure with the possibility of acute complications and long- term chronic complications mainly malnutrition, hypoglycemia and some mental changes. Thus, experts recommend surgical intervention to selected cases when therapeutic lifestyle interventions and pharmacotherapy fail to have adequate control or patients with severe obesity with a body mass index > 30 kg/m^2. (6)

Intensive pharmacological therapy for newly diagnosed type 2 Diabetes:

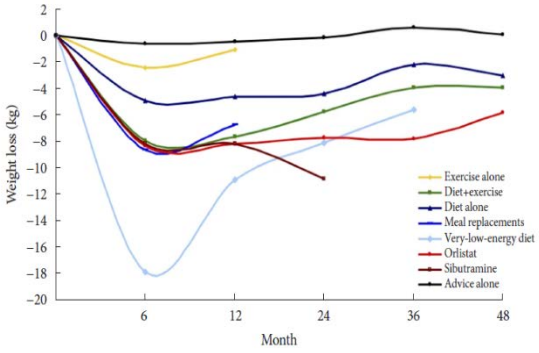
Intensive pharmacological therapy for newly diagnosed type 2 diabetes has shown positive effects on further preservation of β cells functioning. The significant impact of combination therapy in restoring β-cell function is receiving more attention with the development of new drugs.Moreover, several studies confirmed the remission in patients with type 2 diabetes who were newly diagnosed following 2 to 3 weeks of starting intensive insulin



therapy, lasting more than 2 years. (7) It has been also observed, that the earlier insulin therapy is started, the more likelihood of diabetes remission. (8)

Intensive weight reduction with caloric restriction:

Therapeutic lifestyle changes including dietary modification and physical activity remain a cornerstone in the management of diabetes, with favorable effects on body weight and glycemic profile. In a meta- analysis investigating various strategies of weight reduction, the most significant weight loss impact was shown with the very-low-calorie diet (VLCD) with a daily



caloric intake less than 800 kcal, as shown in figure (1). (9)

Average weight change of participants completing at least a 1-year intervention, consisting of a review of 80 studies. Adapted from Franz et al.(9), with permission from Elsevier.

The evidence of newer classes of anti-diabetic medications:

Incretin- based therapy mainly in the form of GLP1 analogues showed excellent weight reduction effects. Among the GLP-1 analogues studied for the preservation of the function of pancreatic β-cell, Liraglutide, newly diagnosed T2DM. (10) Moreover, the dual actions of glucose-dependent insulinotropic polypeptide (GIP) and GLP1- tirzepatide is studied. (11) The drug resulted in a remission rate of 66% to 81%, depending on the drug dose over 52 weeks of use in a clinical study. (12) SGLT2 inhibitors have favorable effects on weight loss and visceral fat reduction due to glucosuria and caloric loss. SGLT2 inhibitors when added to metformin and basal insulin in one study, showed more remission when compared to the conventional group (24.7% vs. 16.9%), and reduced the risk of

diabetes recurrence by 43%. (13). Summary of strategies for type 2 diabetes remission Adapted from Taylor et al. (14), with permission from Portland Press.

Conclusion:

It may be necessary to change the concept of T2DM towards that of an urgent condition that requires rapid intervention rather than a chronic, progressive disease. We must grasp this paradigm shift in our understanding of T2DM for the benefit of our patients as endocrine experts .

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