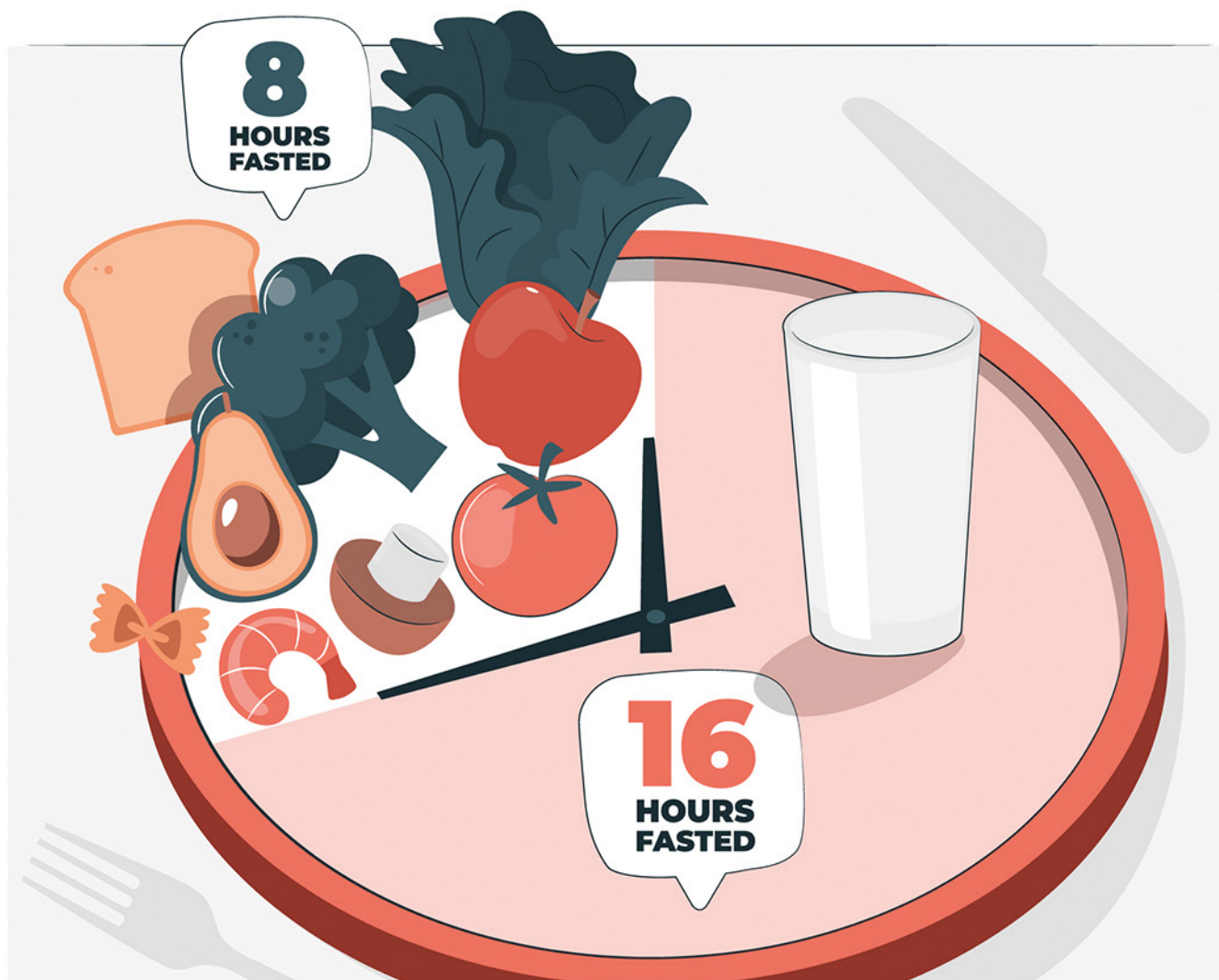




Dra. Alma Prieto Tenreiro.

Specialist in Endocrinology and Nutrition.

Complejo Hospitalario Universitario de Ferrol (A Coruña, Spain).



Intermittent Fasting:

Ally or Risk for Diabetes Control?

Diet is an essential pillar in the management of both type 1 (T1DM) and type 2 diabetes mellitus (T2DM). Although proper nutrition not only helps maintain blood glucose levels within recommended ranges, it also contributes to preventing long-term complications.

In addition to a balanced diet, maintaining a proper body weight is essential. T2DM is closely linked to overweight and obesity, key factors in insulin resistance. However, in recent years, an increase in obesity has also been observed in people with T1DM, leading to the concept of double diabetes. In both cases, weight loss is an essential factor.

Recommendations from major clinical practice guidelines, such as the American Diabetes Association (ADA), emphasize that there is no single eating pattern for people with diabetes (1). Dietary planning should be based on an individualized assessment, taking into account the patient's eating habits, preferences, and metabolic goals. In Spain, the Mediterranean diet (with or without calorie restriction) has traditionally been recommended. This is characterized by a high consumption of minimally processed plant-based foods with olive oil and nuts as the main sources of fat, moderate

consumption of fish, and reduced intake of red and processed meats.

Since there is no universal dietary model for weight control in overweight or obese people or for people with diabetes, intermittent fasting (IF) has aroused increasing interest. In fact, a recent study conducted in Spain has identified an increase in the practice of IF at the expense of the traditional Mediterranean diet, reflecting its acceptance in various sectors of the population. This increase in the popularity of IF is due not only to its possible metabolic benefits but also to the fact that it is a simple, economical, and flexible method, without absolute food restrictions and adaptable to different lifestyles.

WHAT IS INTERMITTENT FASTING?

IF is an eating pattern that alternates periods of free intake with periods of voluntary fasting with total or partial calorie

restriction. Calorie restriction can be done daily during a defined time slot or during complete days (2). During fasting, and unlike other types of religious fasting such as that performed in Ramadan, the free intake of non-caloric liquids such as water, coffee, tea, light broths is allowed. Its most common modalities can be seen in **Table 1**.

THE RISE OF INTERMITTENT FASTING AND ITS GENERAL BENEFITS

In recent years, IF has emerged as one of the most recognized, scientifically explored, and widely promoted diets. Although compared to other eating patterns (such as the Mediterranean diet), the evidence is still limited, more and more studies point to its possible benefits in multiple health conditions such as obesity, cardiovascular disease, or diabetes. An umbrella review conducted by Ming-Li Sun (3) and published in 2024 reported



PROTOCOL	FREQUENCY	DURATION	CONSIDERATIONS
Time-Restricted Eating (TRE)	Every day	Eating window: Maximum of 8 hours of continuous eating per day. Fasting window: Minimum of 16 hours	More restrictive variants limit eating to 4 or 6 hours during the day, with fasting periods of 20 or 18 hours, respectively.
Alternate Day Fasting (ADF)	Every other day	24 hours fasting On fasting days, consumption can range from 0 kcal up to a maximum of 500 kcal. The meal can be consumed all at once or spread throughout the day, based on individual preference.	On eating days, intake is unrestricted.
5:2 Method	2 days a week	24 hours fasting per fasting day. * Fasting days can be consecutive or not. * On fasting days, consumption can range from 0 kcal up to a maximum of 1000 kcal. The meal can be consumed all at once or spread throughout the day, based on individual preference	On the other 5 days, intake is unrestricted.

Table 1. Most common types of intermittent fasting

INTERMITTENT FASTING IS GAINING POPULARITY IN SPAIN AND WORLDWIDE AS A POTENTIAL STRATEGY FOR METABOLIC CONTROL AND WEIGHT LOSS

» that IF is associated with several benefits shown in **Figure 1**.

INTERMITTENT FASTING AND THE “METABOLIC SWITCH”

And how would IF achieve these effects? Emerging findings suggest that the benefits of IF would be independent of weight loss. These would be based on the “metabolic switch,” which can be explained as the change in the use of glucose as the main energy source towards a preferential use of ketone bodies from fatty acid oxidation and an increase in autophagy and stress resistance. Despite these possible benefits, IF has not been shown to be superior to traditional continuous calorie restriction.

FROM RISK TO POSSIBLE ALLY IN DIABETES: EVOLUTION OF THE PERCEPTION OF INTERMITTENT FASTING

Historically, IF has been considered a risky practice for people with DM due to concerns

about the potential risk of hypoglycemia, the possibility of diabetic ketoacidosis (DKA) in people with T1DM, and difficulties in adapting pharmacological treatment. However, in recent years, the accumulation of studies has led to a change in clinical perception, with a growing interest in its potential metabolic benefit in both T1DM and T2DM.

The 2019 ADA consensus (3) already mentioned the rise of IF as a dietary option with possible benefits in weight loss and glycemic control, although it pointed out that the evidence at that time was too limited to establish recommendations. Since then, research has advanced, consolidating its usefulness in certain contexts.

EVIDENCE IN TYPE 2 DIABETES MELLITUS

Several studies have evaluated the impact of IF in people with T2DM, the most impactful being:

- INTERFAST-2 study (2023): in patients with T2DM treated with insulin with insufficient metabolic control (HbA1c >7%), »



FIGURE 1. Benefits of intermittent fasting

Benefits in Body Composition:

Reduction in body weight and visceral fat, with improvement in lean body mass.

Glycemic Benefits:

Decreases fasting insulin levels and improves insulin sensitivity.

Lipid Benefits:

Decreases total cholesterol, LDL cholesterol, and triglycerides.

Cardiovascular Benefits:

Decreases systolic blood pressure.

- » 3 days of IF per week for 12 weeks significantly reduced HbA1c, body weight, and total insulin dose without increasing the risk of hypoglycemia and increasing quality of life.
- EARLY study (2024): in people with early diabetes, IF performed using the 5:2 method showed greater effectiveness in reducing HbA1c and weight vs metformin and empagliflozin.
- A systematic review and meta-analysis published in 2024 by Mousa K. concluded that in patients with prediabetes and T2DM without insulin, IF improves weight, body mass index, and glycemic control.
- A systematic review and meta-analysis published in 2021 by Wang X. concluded that in patients with T2DM and metabolic syndrome, IF achieves a reduction in HbA1c, glycemia, and fasting insulin similar to that achieved with a traditional hypocaloric diet, although a slightly greater weight loss.

EVIDENCE IN TYPE 1 DIABETES MELLITUS

Evidence on IF in T1DM is even more limited, often with inferences made from studies in patients with religious fasting such as Ramadan. Some of the most notable are:

- In a small study by Overland J. published in 2021, in patients with T1DM and overweight/obesity, both IF and the traditional hypocaloric diet achieved similar results in safe weight loss.
- A review by Varady KA. published in 2018 concluded that IF can be an effective strategy in patients with T1DM and obesity, improving HbA1c and weight.
- A review by Herz D. in 2023, which evaluated the efficacy of IF in patients with T1DM and T2DM, concluded that in patients with T1DM, IF has the potential to minimize the risk of hypoglycemia and decrease glycemic variability, increasing insulin sensitivity and reducing body weight.

RISKS AND CONSIDERATIONS

Although performing IF may present bene-»



ALTHOUGH INTERMITTENT FASTING MAY OFFER BENEFITS FOR PEOPLE WITH DIABETES, IT ALSO PRESENTS SIGNIFICANT RISKS AND CHALLENGES. THEREFORE, IT IS ESSENTIAL THAT IT BE CONDUCTED UNDER MEDICAL SUPERVISION



- » fits in people with diabetes, it also presents significant risks and challenges, so it is essential that it be done under medical supervision. Among its possible risks are:
 - Risk of hypoglycemia, especially in T1DM and in patients on insulin or sulfonylureas.
 - Possibility of DKA in T1DM if insulin is not adjusted correctly. For this reason, it is advisable to routinely monitor capillary ketonemia when starting IF.
 - Difficulties in long-term adherence, which can impact treatment sustainability.
- In addition, some populations are especially vulnerable and entail unique risks. For this reason, IF is contraindicated in pregnant and lactating women, young children, elderly and/or frail adults, people with immunodeficiencies, and people with eating disorders in whom harmful behaviors could be exacerbated by performing IF. In addition, in the specific »

» case of people with diabetes, IF is discouraged in case of poor metabolic control or a history of severe hypoglycemia. Likewise, extreme precautions should be taken in patients with diabetes and other serious comorbidities.

PRACTICAL RECOMMENDATIONS FOR IMPLEMENTATION

For safe implementation of IF in people with diabetes, the following recommendations based on expert opinions are suggested:

- 1. Specialized supervision:** people with diabetes mellitus interested in IF should do so under the guidance of a health professional, such as doctors, specialized nurses, or registered dietitians.
- 2. Drug adjustment:** although there are no specific clinical guidelines for treatment adaptation, during IF, it is necessary to reduce insulin doses and some hypoglycemic agents.
- 3. Use of continuous glucose monitoring (CGM) systems:** CGM is recommended to prevent and detect hypoglycemia episodes early, especially in patients with T1DM or on insulin treatment.
- 4. Planning of feeding windows:** ensure a balanced intake during feeding periods, prioritizing the intake of proteins, healthy fats, and fiber.
- 5. Adequate hydration:** although patients can consume non-caloric liquids during fasting, by reducing the intake of foods with high water content (such as soups, yogurts, or fruits), the risk of dehydration and hypotension may increase, which may require adjustments in other treatments, such as diuretics, SGLT-2 inhibitors, or antihypertensives. **D**

CONCLUSIONS

Intermittent fasting has gone from being a strategy considered risky to an option with potential in the management of diabetes. Evidence suggests that it could contribute to improving glycemic control, reducing body weight, and decreasing insulin requirements safely. However, the available studies are still limited, with few patients, short duration, and methodological heterogeneity, which prevents establishing firm recommendations. In addition, the absence of standardized clinical guidelines hinders its implementation at the clinical level. More robust and longer studies are required to confirm its possible benefits and ensure its safety.

Until there is more evidence, it cannot be recommended in a generalized way and should be implemented individually, always under medical supervision. This is especially relevant in people with T1DM or on insulin treatment, who require frequent monitoring and adjustments in their treatment to minimize risks and optimize benefits

REFERENCES

1. Evert AB, Dennison M, Gardner CD, Garvey WT, Lau KHK, MacLeod J, et al. Nutrition Therapy for Adults With Diabetes or Prediabetes: A Consensus Report. *Diabetes Care*. 2019 May;42(5):731-754.
2. Varady KA, Cienfuegos S, Ezpeleta M, Gabel K. Clinical application of intermittent fasting for weight loss: progress and future directions. *Nat Rev Endocrinol*. 2022 May;18(5):309-321.
3. Sun ML, Yao W, Wang XY, Gao S, Varady KA, Forslund SK et al. Intermittent fasting and health outcomes: an umbrella review of systematic reviews and meta-analyses of randomised controlled trials. *EclinicalMedicine*. 2024 Mar 11;70:102519.
4. Obermayer A, Tripolt NJ, Pferschy PN, Kojzar H, Aziz F, Müller A, et al. Efficacy and Safety of Intermittent Fasting in People With Insulin-Treated Type 2 Diabetes (INTERFAST-2)-A Randomized Controlled Trial. *Diabetes Care*. 2023 Feb 1;46(2):463-468.
5. 3Guo L, Xi Y, Jin W, Yuan H, Qin G, Chen S, et al. A 5:2 Intermittent Fasting Meal Replacement Diet and Glycemic Control for Adults With Diabetes: The EARLY Randomized Clinical Trial. *JAMA Netw Open*. 2024 Jun 3;7(6):e2416786.
6. Khalafi M, Habibi Maleki A, Symonds ME, Rosenkranz SK, Rohani H, Ehsaniifar M. The effects of intermittent fasting on body composition and cardiometabolic health in adults with prediabetes or type 2 diabetes: A systematic review and meta-analysis. *Diabetes Obes Metab*. 2024 Sep;26(9):3830-3841.
7. Wang X, Li Q, Liu Y, Jiang H, Chen W. Intermittent fasting versus continuous energy-restricted diet for patients with type 2 diabetes mellitus and metabolic syndrome for glycemic control: A systematic review and meta-analysis of randomized controlled trials. *Diabetes Res Clin Pract*. 2021 Sep;179:109003.
8. Overland J, Toth K, Gibson A, Sainsbury A, Franklin J, Gauld A et al. The safety and efficacy of weight loss via intermittent fasting or standard daily energy restriction in adults with type 1 diabetes and overweight or obesity: A pilot study. *Obesity Medicine* 12 (2018) 13–17.
9. Varady KA, Runcney MC, Reutrakul S, Vidmar AP, Chow LS. Clinical potential of fasting in type 1 diabetes. *Trends Endocrinol Metab*. 2024 May;35(5):413-424.
10. Herz D, Haupt S, Zimmer RT, Wachsmuth NB, Schierbauer J, Zimmermann P, et al. Efficacy of Fasting in Type 1 and Type 2 Diabetes Mellitus: A Narrative Review. *Nutrients*. 2023 Aug 10;15(16):3525.