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Original Article

Adherence to the mediterranean diet and risk of hypoglycemia in insulin-treated type 2 diabetic patients

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ABSTRACT

Background and aims: Lifestyle intervention, aimed at weight loss and increasing physical activity, is widely known as the first-line treatment in diabetes. Adherence to a medical nutritional therapy (MNT) is even more relevant in patients on insulin therapy. However, data on the relationship between diet composition and glycemic control indexes derived from continuous glucose monitoring (CGM) in type 2 diabetes (T2D) are scarce and inconsistent. Our aim was to evaluate the association between adherence do Mediterranean diet (MD) and CGM metrics in a cohort of T2D patients treated with insulin.

Methods and results: We retrospectively collected data of 25 patients with T2D on insulin therapy, at the Diabetes Unit of University Hospital in Siena. They were prescribed a flash glucose monitoring (FGM) system and accepted to answer the MEDLIFE questionnaire, a validated tool designed to explore the adherence to MD. Adherence to MD did not seem to influence glycemic control indexes in our cohort. It is worth mentioning that the risk of hypoglycemia and time spent in hypoglycemia was found to be highly influenced by alcohol consumption, even in minimal amounts (according to national guideline recommendations).

Conclusion: Nutritional counselling for patients with insulin-treated T2DM should include a focus on alcohol consumption – ideally to be avoided - and related hypoglycemic risk.

1. Introduction

In recent decades, the prevalence of type 2 diabetes (T2D) has rapidly increased, with an increasing number of patients developing long-term diabetes-related complications and requiring insulin therapy for disease management [1,2]. This trend has turned T2D into a global concern in terms of healthcare costs and the loss of human resources. According to the International Diabetes Federation (IDF), approximately 9.3 % of adults worldwide had diabetes in 2019, and this number is expected to reach 700 million by 2045 [3].

Given the well-established link between hyperglycemia and the development of complications, optimizing glycemic control has become a key priority [4]. In this scenario, medical nutritional therapy (MNT) plays a pivotal role, representing the first line treatment for diabetes [5–7]. Previous studies have demonstrated the efficacy of intensive lifestyle interventions aimed at weight loss (WL) and increasing physical activity (PA) in both preventing and managing T2D [8–12].

Several dietary patterns have been suggested for managing diabetes. Although a personalized approach - tailored to both macronutrient distribution and caloric intake - is always preferred, the Mediterranean Diet (MD) is widely recommended. This diet emphasizes minimally processed foods, including fruits, vegetables, whole grains and legumes, fish, poultry and skimmed dairy products as sources of protein, and olive oil and oilseeds as sources of fat [13]. The benefits of MD in diabetes mellitus have been widely recognized. However, while studies comparing various dietary patterns are limited, in recent years, “alternative” diets (e.g., ketogenic, high-protein, low-carb, etc.) have gained increasing attention, thanks to their good short-term effects on glycemic control and weight loss. Nevertheless, long-term outcomes for A1c, fasting blood glucose, and insulin use still favor MD [14–19]. MD has

Abbreviations: A1c, glycated hemoglobin; CHO, carbohydrate; CGM, continuous glucose monitoring; CVD, cardiovascular diseases; FGM, flash glucose monitoring; MD, Mediterranean diet; MNT, medical nutritional therapy; PA, physical activity; T1D, type 1 diabetes; T2D, type 2 diabetes; TAR, time above range; TBR, time below range; TIR, time in range; IDF, International Diabetes Federation; WFKD, well-formulated ketogenic diet; WL, weight loss.

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also proven to be an excellent prevention tool in individuals at risk of developing T2D. The PREDIMED study first demonstrated that MD reduced the risk of T2D occurrence by 52 % in nondiabetic subjects [20,21] and subsequent studies confirmed that higher MD adherence significantly lowers the risk of T2D [22,23]. MD has also been extensively studied in the prevention of cardiovascular diseases (CVD). As early as the 1960s, Ancel Keys' "Seven Countries Study" revealed that Mediterranean populations had a lower incidence of CVD, linking this finding to dietary habits. The impressive work of Keys and colleagues led to the definition of the Mediterranean diet, which is now recognized as a means to improve health and reduce cardiometabolic risk. Subsequent evidence, although limited and variable, confirmed this hypothesis [24].

In T2D patients, the start of insulin therapy does not undermine the importance of MNT. On the contrary, adherence to specific dietary measures becomes even more crucial to avoid both hypoglycemic and hyperglycemic events.

Basal-bolus insulin therapy presents challenges for patients, particularly the fear of hypoglycemia and the need for intensive blood glucose monitoring. The advent of continuous glucose monitoring systems (e.g., flash glucose monitoring, FGM, and continuous glucose monitoring, CGM) has significantly improved patients quality of life and glycemic control and provided new parameters to evaluate glycemic control [25,26]. These indexes include time in range (TIR), which indicates the length of time the patient spends within the target range of glycemia (between 70 mg/dl and 180 mg/dl), time above range (TAR), indicating the duration of hyperglycemia and time below range (TBR), a marker of the number of hypoglycemic events. In addition, the system provides an estimated A1c as well as information about the glycemic variability [27].

Carbohydrate (CHO) intake is the major determinant of postprandial glycemia (PPG), with higher CHO intake is associated with poorer glycemic control. Therefore, a correlation between diet composition and FGM/CGM-derived parameters is strongly conceivable. In younger patients with type 1 diabetes (T1D), Dominguez-Riscart et al. [28] demonstrated a positive correlation between TIR and adherence to MD, assessed with the KIDMED questionnaire. Similarly, Levran et al. [29] reported an improvement of TIR after a 6-month dietary intervention in T1D patients. Other studies found correlations between dietary components and glucose variability in T1D, suggesting that a CHO intake of no more than 50 % of total calories and 15 % of protein helps reduce glycemic fluctuations [30]. In T2D patients, data on the association between diet composition or adherence and TIR are scarce and inconsistent. A recent study evaluating the impact of diet on glucose monitoring parameters showed that adequate protein intake increases TIR and decreases TAR, while excessive CHO consumption negatively affects TIR [31]. However, authors focused solely on macronutrients composition, and their findings were inconsistent with a similar report on a T2D Japanese cohort where no significant association was found between a low-carbohydrate-diet score evaluated through BDHQ questionnaire and glycemic control indexes [32]. Gardner and colleagues demonstrated a similar effect on A1c reduction and TIR improvement in a crossover trial comparing a well-formulated ketogenic diet (WFKD) and MD in prediabetes and T2D, concluding that reducing CHO intake has beneficial effects on glucose levels [33].

Our study aimed to evaluate the association between MD adherence and FGM metrics in a cohort of insulin-treated T2D patients.

2. Methods

We enrolled twenty-five consecutive insulin-treated T2D patients (20 males, 5 females) at Diabetes and Metabolic Disease Unit of the University Hospital in Siena. Patients were treated with basal bolus insulin regimen, either alone or in combination with other antihyperglycemic drugs, and were using FGM monitoring. The study was conducted according to the guidelines of the Declaration of Helsinki and approved by local Ethics Committee. Informed consent was obtained from all participants.

At diagnosis, all patients received dietary education, with periodic re-evaluation as needed during follow-up. All patients were provided FGM for glycemic monitoring. FGM metrics analyzed are summarized in Table 1 and were evaluated according to the targets set by Battelino et al [27]. All clinical visits and therapy modifications were conducted according to good clinical practice.

MD adherence was evaluated by MEDLIFE questionnaire, a validated tool designed to explore adherence to the Mediterranean Diet Pyramid through twenty-eight items, divided into three blocks: food consumption frequency (15 items), Mediterranean dietary habits (7 items) and physical activity, rest, social habits and conviviality (6 items). Each item scored 0 or 1, so that the final score ranges from 0 (worst adherence) to 28 (perfect adherence) [34,35].

Statistical analysis was performed with GraphPad Prism vers. 8.1.1. (GraphPad Prism, La Jolla, CA, USA). Mann-Whitney *U* test and Wilcoxon test or Kruskal-Wallis with Dunn's post-test were used to determine differences between two or more groups, respectively. Chi-square test was used to compare variables among categories. Linear regression analysis using Spearman R test was used as correlation test to assess the link between clinical and FGM parameters and MEDLIFE results. To assess the potential impact of confounding factors, a multivariate statistical analysis was performed. Separate beta regression models were fitted for each outcome variable (severe TBR%, mild-to-moderate TBR %, and overall TBR%) to identify significant differences across patient stratifications (Drinkers/Non-Drinkers; 0–1 Glasses/≥2 Glasses). The outcome variables were treated as the dependent variable in each model, while patient stratification and confounding factors (disease

Table 1
Baseline characteristics.

	Mean ± SD	Range	yes/no (%)
Age (y)	67,2 ± 10,1	49–96	–
Age at FGM prescription (y)	61,6 ± 9,1	48–80	–
Duration of disease (y)	18,2 ± 14,1	2–50	–
BMI (kg/m^2)	29,7 ± 6,3	20.2–86	–
Insulin dose (IU/kg)	0,6 ± 0,4	0.2–1.7	–
A1c (%)	7,8 ± 1,6	4.8–13.3	–
FPG (mg/dl)	148,5 ± 47,8	71–248	–
Total cholesterol (mg/dl)	159,0 ± 50,5	94–293	–
Triglycerides (mg/dl)	165,5 ± 134,0	50–663	–
HDL cholesterol (mg/dl)	44,2 ± 11,5	27–69	–
LDL cholesterol (mg/dl)	82,9 ± 41,2	25–208.8	–
Creatinine (mg/dl)	1,3 ± 0,9	0.6–4.7	–
GFR CKD-EPI (ml/min/1.73m^2)	69,0 ± 24,6	27–111.9	–
Urinary albumin (mg/l)	149,2 ± 312,5	0–1166	–
TIR (%)	60,1 ± 26,3	0–97	–
TAR 180–250 (%)	26,4 ± 16,3	2–60	–
TAR > 250 (%)	12,1 ± 18,9	0–86	–
TBR > 30 (%)	1,3 ± 3,3	0–16	–
TBR < 30 (%)	0,2 ± 0,4	0–1	–
GMI (%)	7,4 ± 0,9	5.8–9	–
Variability Index (%)	27,1 ± 6,5	15.6–38.5	–
Number of hypoglycemic events (14d)	2,2 ± 4,7	0–20	–
Estimated A1c (mmol/mol)	57,5 ± 9,6	40–75	–
Use of sensor (%)	79,7 ± 29,8	10–100	–
Presence of nephropathy	–	–	13/25 (52 %)
Presence of diabetic retinopathy	–	–	5/25 (20 %)
Presence of cardiovascular diseases	–	–	9/25 (36)
Arterial hypertension (AH)	–	–	18/25 (72 %)
Peripheral neuropathy or diabetic foot	–	–	4/25 (16 %)
At least one complication (AH excluded)	–	–	15/25 (60 %)

duration, presence of comorbidities, age, and insulin dose per Kg) were included as predictors. Beta regression model was chosen due to its suitability for proportion-based dependent variables. Outcomes were rescaled to the (0, 1) interval using the Smithson and Verkuilen method [36]. To determine the significance of association between clinical outcome and stratification, the p-value associated with stratification was assessed after adjusting for confounding variables. P-values below 0.05 were considered statistically significant.

2.1. Study population

Patient characteristics are shown in Table 1.

3. Results

When analyzing the FGM-derived AGP reports, patients did not meet the optimal FGM targets, with lower average TIR% and higher average TAR% than recommended, though the mean TBR% was acceptable (Table 1). Ten patients (40 %) displayed an adequate TIR% (>70 %) and only 5 patients (20 %) reached the A1c target of 53 mmol/mol; however, one of these patients had a markedly high TBR% (17 %). It is worth noting that some patients exhibited a poor compliance to FGM monitoring, with less than 50 % of the recommended use. The results obtained in the MEDLIFE questionnaire and the respective FGM parameters of each individual patient are shown in Table S1.

Results of the questionnaires showed a relatively poor adherence to MD (mean score ± SD 16,2 ± 3,1, range 10–22), and none of the participants obtained the maximum score. Most participants (76 %) were in the middle tertile (score 11–19), only 4 patients (16 %) scored in the highest tertile (score 20–28) and 2 (8 %) in the lowest tertile (score 1–10).

In order to provide an overall picture of our population, we evaluated the distribution of results over the individual items of the questionnaire. Key deviations from the MD recommendation in consumption frequencies (block 1) included inadequate fruit intake (only 20 % of those surveyed consumed at least 3 servings per day), dairy consumption (only 16 % of the sample met the indications), and legumes and nuts (64 % of the patients did not consume the recommended servings). Considering the Mediterranean dietary habits (block 2), the most common errors included insufficient water intake, wine consumption and whole grains intake. Finally, regarding block 3 items, none of the selected patients played team sports, and only 24 % of patients practiced recommended PA, while about 3 quarters of the sample reported watching TV far longer than recommended (Table 2).

In our cohort, no clear correlation was found between MEDLIFE questionnaire scores and FGM parameters, nor differences in FGM metrics when comparing the different tertiles of MEDLIFE scores. However, linear regression analysis showed a non-significant trend toward an inverse correlation between MEDLIFE score and level 2 TAR and TBR, and patients in the lowest tertile of MEDLIFE scores showed a higher percentage of time spent with glycemia >250 mg/dl, suggesting that a better MD adherence could be associated to a lower risk of hypoglycemia and severe hyperglycemia (Fig. S1).

When considering scores obtained in each of the three blocks composing MEDLIFE questionnaires, block 3 scores, were inversely correlated with age. This is a plausible result since PA and sociality is usually higher in young people, while block 2 scores showed a trend toward negative correlation with A1c (Fig. 1). Block 3 scores also showed a non-significant trend for positive correlation with BMI. It could be speculated that patients with obesity are encouraged to engage in more activities to lose weight. Patients who scored higher in block 1 and 2 showed lower insulin dose, patients with higher score in block 1 showed a slightly lower FPG and TBR% values, while higher scores in block 2 were seen in patients with lower A1c, FPG, TAR% and higher TIR % values. None of these differences, though, reached the statistical significance (data not shown).

Table 2
MEDLIFE scores.

	Criteria for 1 point[a]	Patients scoring 1 point n (%)	Patients scoring 0 point n (%)
Sweets	≤2 servings/week	20 (80)	5 (20)
Red Meat	<2 servings/week	20 (80)	5 (20)
Processed Meat	≤1 serving/week	13 (52)	12 (48)
Eggs	2-4 servings/week	13 (52)	12 (48)
Legumes	≥2 servings/week	9 (36)	16 (64)
White Meat	2 servings/week	18 (72)	7 (28)
Fish/seafood	≥2 servings/week	15 (60)	10 (40)
Potatoes	≤3 servings/week	23 (92)	2 (8)
Dairy products	2 servings/d	6 (24)	19 (76)
Nuts/Olives	1-2 servings/d	9 (36)	16 (64)
Herbs, spices	≥1 servings/d	17 (68)	8 (32)
Fruit	3-6 servings/d	5 (20)	20(80)
Vegetables	≥2 servings/d	19 (76)	6 (24)
Olive oil	≥3 servings/d	16 (64)	9 (36)
Cereals	3-6 servings/d	15 (60)	10 (40)
Water	6–8 glasses/d	9 (36)	16 (64)
Wine	1-2 glasses/d	6 (24)	19 (76) [b]
Limit Salt	Yes	19 (76)	6 (24)
Preference for wholegrain products	Yes (fiber >25 g/d)	7 (28)	18 (72)
Snacks	≤2 servings/week	21 (84)	4 (16)
Limit Nibbling	Yes	16 (64)	9 (36)
Limit sugar in beverages	Yes	23 (92)	2 (8)
Physical Activity	Yes (150 min/week or 30 min/d)	6 (24)	19 (76)
Naps	Yes	15 (60)	10 (40)
Hours of sleep	6–8 h/d	23 (92)	2 (8)
Watching television	<1 h/d	7 (28)	18 (72)
Socializing with friends	≥2 h/weekend	16 (64)	9 (36)
Collective sports	≥2 h/week	0	25 (100)

[a] Criteria for 1 point are derived from Sotos-Prieto et al. (32): 1 point is obtained if criterion is met, 0 point if not met.
[b] Patients scoring 0 points in this item do not consume wine at all (0 glass/d) or consume less than half glass/d.

Healthier dietary choices, as per MD recommendations, did not seem to significantly affect FGM metrics, without significant differences in FGM-derived parameters between patients consuming adequate or inadequate quantities of different foods or having healthier habits, as investigated by MEDLIFE. However, some associations of potential interest are worth noting. Patients using less olive oil as seasoning (less than 3 spoons daily) needed significantly higher insulin dose/kg of body weight (Fig. 2). Interestingly, patients consuming very low quantities of fruits (less than 2 servings per day) showed significantly worse TIR%, global TAR% and level 2 TAR% (Fig. 2). As for PA, patients who exercised regularly had longer total and mild-to-moderate TBR%, without severe hypoglycaemic episodes (Fig. 2). Surprisingly, PA did not seem to significantly improve overall glycemic control, with no significant difference between active and less active patients in terms of TIR%, level 1 TAR%, level 2 TAR%, GMI, and A1c (data not shown). Regarding social habits, patients taking naps in the afternoon showed significantly worse A1c, while FGM parameters were not significantly affected (Fig. 2).

Drinking wine at meals (more than one glass of wine daily) did not affect TIR%, level 1 TAR%, level 2 TAR%, GMI, A1c and variability index (data not shown). However, we found that patients regularly drinking more wine showed a tendency for higher overall TBR% and severe TBR% (Fig. 3). Interestingly, when patients were classified

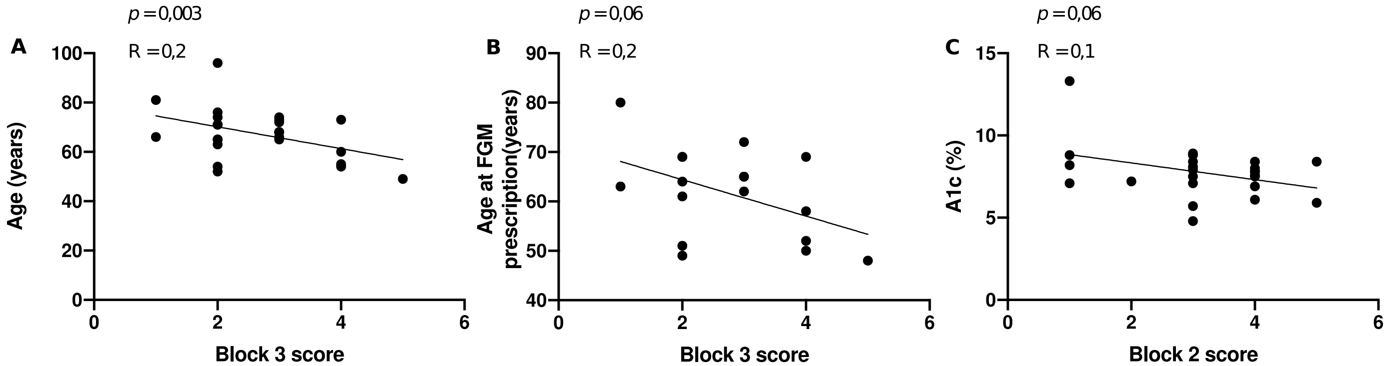

Fig. 1. MD adherence and clinical parameters. Dot plot graphs of correlations between Block 3 score and age (A) and age at FGM prescription (B); dot plot graphs of correlation between Block 2 score and A1c (C). Statistics using linear regression.

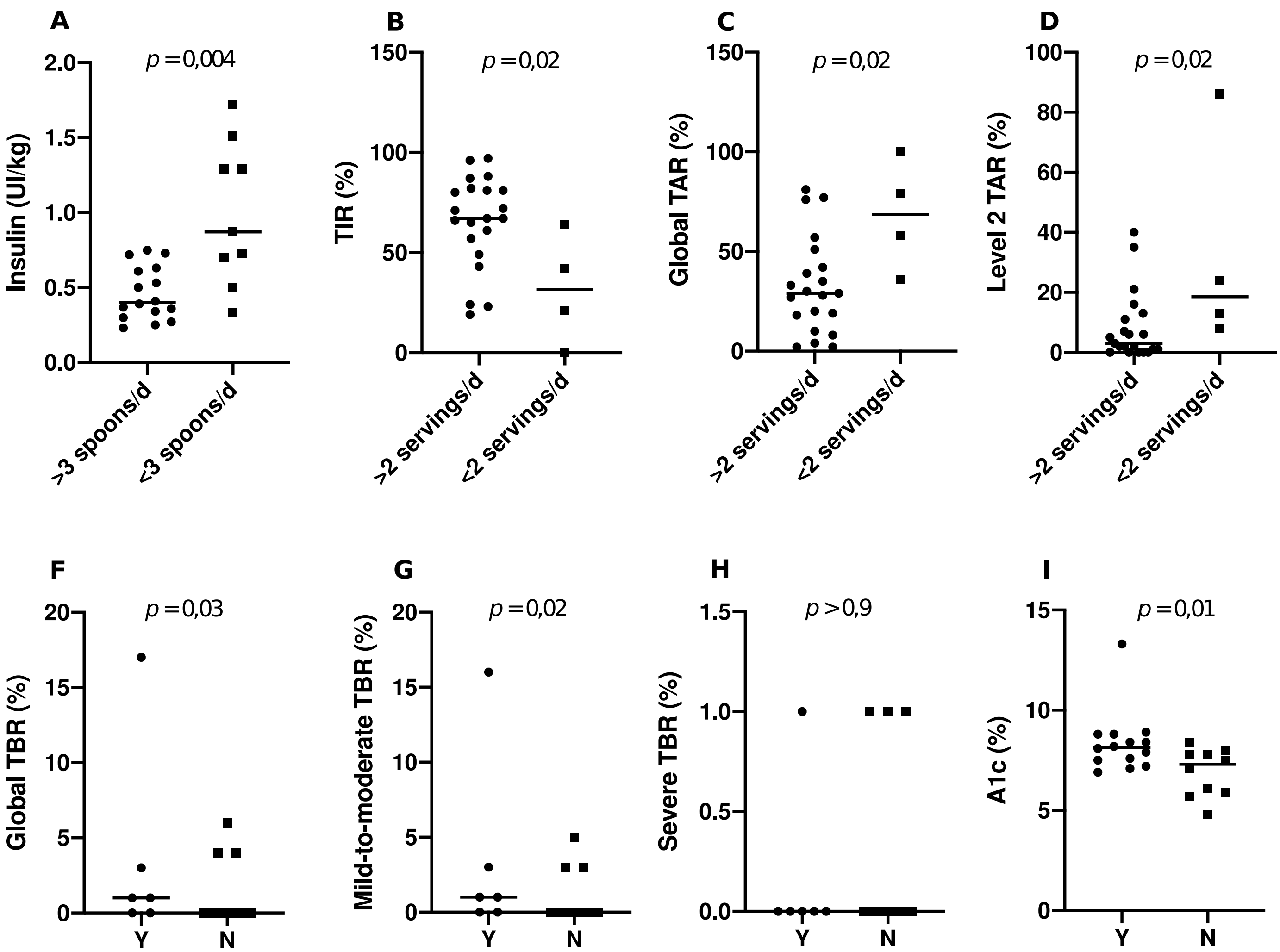

Fig. 2. Lifestyle and glycemic control. Comparison of insulin dose per kg between patients using more or less than 3 spoons of olive oil/d (A), TIR% (B), TAR% (C) and level 2 TAR% (D) between patients consuming more or less than 2 servings of fruit per day, TBR% (E), mild-to-moderate TBR% (30–70 mg/dl) (F) and severe TBR % (<30 mg/dl) (G) between patients performing PA versus inactive patients, A1c (%) levels between patients used to afternoon naps or not (H). Statistics using Mann-Whitney test.

according to their drinking habits into non-drinkers (i.e., 0 units of total alcohol consumption per day), and regular drinkers, drinking at least one glass of wine per day, the relationship between alcohol consumption and hypoglycemia was confirmed, reaching statistical significance. Indeed, we found that drinkers have a higher risk of hypoglycemia, with significantly higher global TBR%, mild-to-moderate TBR% and severe TBR% (Fig. 3).

In order to exclude the effect of confounding factors, we performed a multivariate statistical analysis, which confirmed that, regardless of several confounding factors (age, disease duration, presence of diabetes-related comorbidities and intensity of insulin therapy), drinking less than two glasses of wine is associated with lower risk of hypoglycemia in

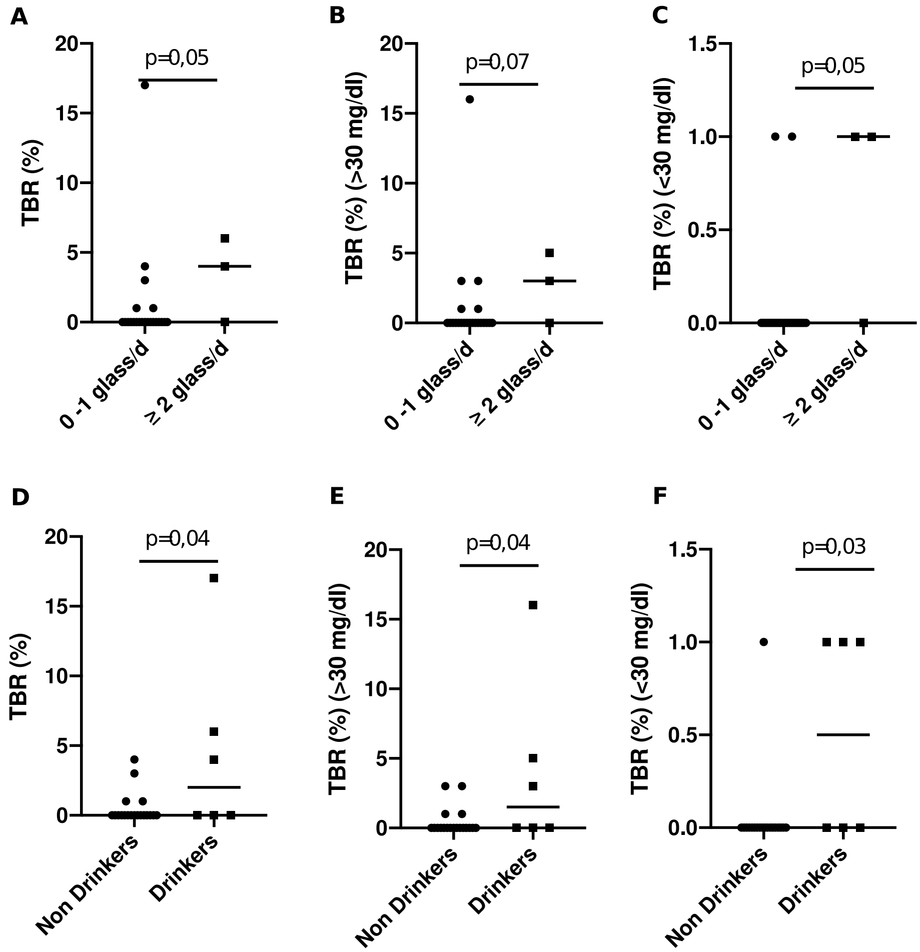

Fig. 3. Alcohol and glycemic control. Upper panel: comparison of TBR% (A), mild-to-moderate TBR% (B) and severe TBR% (C) between patients consuming more or less than 1 glass of wine per day. Lower panel: comparison of TBR% (D), mild-to-moderate TBR% (E) and severe TBR% (F) between nondrinkers and drinkers. Statistics using Mann-Whitney test.

terms of global TBR%, mild-to-moderate TBR%, severe TBR%. Similarly, drinking wine (even in small quantities) was confirmed to increase the risk of hypoglycemia, in terms of global TBR%, mild-to-moderate TBR% and severe TBR%, independent of the evaluated confounding factors (Table S2-S3).

4. Discussion

Diabetes mellitus is a heterogeneous disease with a wide range of clinical manifestation, whose prevalence is rapidly increasing, making it a global epidemic. The increasing prevalence of diabetes pose significant health and socioeconomic challenges worldwide, given the increased morbidity and mortality associated with the disease. Strategies to achieve good glycemic control, and thereby reduce the risk of complications, include various pharmacological and non-pharmacological intervention. Among the latter, MNT has a key role in controlling glycemic excursions. While there is no definitive evidence favoring one specific dietary pattern over another, a substantial body of research supports the role of MD in improving glycemic control and reducing the risk of cardiovascular events [21,37,38]. Although MNT should be considered as the first-line therapy in T2D, it becomes even more important in patients on insulin therapy. Since MNT is strongly suggested in combination with insulin to reduce glycemic fluctuations, good adherence to dietary advice should improve glycemic control indexes, including parameters derived from interstitial glucose monitoring.

In the sample analyzed, adherence to MD was suboptimal. Indeed, less than a quarter of the subjects scored in the upper tertile, indicating good adherence. The main deviations from the national dietary guidelines - based on the MD model - included consumption of fruits, legumes, whole grains and dairy products, found to be inadequate in more than half of the patients surveyed. Additionally, approximately 70 % of the patients reported time spent in front of TV exceeding recommendations. However, surprisingly, the scores obtained in the MEDLIFE questionnaire did not seem to affect FGM metrics, suggesting that, in this category of patients, adherence to MD does not significantly affect glycemic control. Despite this result seems at odds with much of the existing literature, where diet is reported to have a positive impact on glycemic control, we cannot rule out the possibility that insulin-treated patients may have more severe and long-standing disease, making dietary intervention less impactful in this specific category of patients. In addition, patients treated with insulin may be prioritize pharmacological correction of hyperglycemia over dietary measures. However, the suboptimal adherence to MD in our cohort does not allow us to draw firm conclusions, but it does suggest the importance of periodic educational reinforcement on proper lifestyle, especially eating habits, even in patients with longer disease duration and treated with insulin.

Of note, we found some interesting associations between certain foods consumption and clinical and FGM-derived parameters. Specifically, lower fruit consumption was associated with worse glucose control as measured by FGM. This result is somewhat perplexing: given the high content of sugars in fruit, one could expect that lower consumptions would reduce hyperglycemic peaks. However, a recent meta-analysis showed that fruit consumption is associated with a significant reduction in FPG, without affecting A1c, suggesting a beneficial effect of increasing fruit intake, without changing the total caloric intake [39]. In addition, timing of fruit consumption (i.e. at the end or between main meals) may have a different effect on glycemic excursion, although this is not specifically addressed by the MEDLIFE questionnaire. Moreover, patients consuming higher quantities of fruits might be less likely to eat sweet or savory snacks: indeed, in our cohort, 75 % of patients consuming less fruits reported eating sweets more than twice per week.

The association between lower olive oil consumption and higher insulin dose is also quite challenging to explain. Although not specifically addressed by the MEDLIFE questionnaire, we could speculate that patients consuming less olive oil may choose other seasonings, like animal-derived fats or commercial sauces, rich in saturated fats (SFA), with detrimental effects on LDL-cholesterol levels and CVD risk. Although the impact of SFA intake on risk and glycemic control is still debated [40], it is well-established that mono- and polyunsaturated fats has a role in preserving insulin sensitivity, while SFA-rich diets favor the onset of insulin resistance [41].

Alcohol consumption seems to significantly influence both severe and mild-to-moderate hypoglycemic events, with a higher time spent in hypoglycemia in patients who consume wine, albeit in recommended amounts. The impact of alcohol on the risk of hypoglycemia is widely known, but these findings suggest that patients treated with insulin should be more cautious and receive tailored education on alcohol consumption - ideally avoiding it. The risks and harms associated with drinking alcohol are well documented, particularly in vulnerable populations, with higher rates of alcohol-related death and hospitalization. Besides, the World Health Organization has recently declared that when it comes to alcohol consumption, there is no safe amount that does not affect health [42].

Regarding PA, in our sample the most active patients were more prone to hypoglycemia, which may suggest a lack of knowledge regarding pre- and post-exercise strategies such as reduction of insulin doses, adequate consumption of simple and complex carbohydrates before, during and after exercise, preferably to be scheduled. Again, this highlights the need for proper patient education, to ensure better management of meals and therapy during PA, which should always be encouraged. Lastly, the evidence of worse A1c levels in patients taking afternoon naps should be interpreted with caution, given the many possible confounding factors (e.g., the habit of eating more complex, difficult-to-digest meals at lunch, impaired sleep quality and concomitant higher daytime sleepiness due to OSAS, use of sleep-inducing drugs). Unfortunately, the MEDLIFE questionnaire did not specifically analyze these factors, so the explanation the explanation for this finding remains speculative.

Limitations of the study include the small sample size, which does not allow generalizable conclusions. Furthermore, we cannot exclude that the gender imbalance in our population may introduce a possible gender bias in the evaluation of metabolic parameters. It should be emphasized that the assessment of nutritional habits is challenging because the impact of a single hypothetical risk factor usually takes time to show up and cannot be evaluated in the short term. Furthermore, the cross-sectional design of the study does not allow conclusions on the effect of over time, restricting conclusions to associations, rather than causality. Moreover, the questionnaire does not specifically investigate the timing of single food consumption (*e.g.*fruit), the macronutrients content of meals and ingestion order, the carbohydrate intake or meal timing, the consumption of different types of alcoholic beverages, all of which may affect post-prandial glycemia. Finally, it is important to consider the intrinsic limit of data obtained from self-reported questionnaires. While these preliminary results remain unconfirmed on a larger scale, they provide us with some food for thought on the management of T2D patients treated with insulin and the nutritional recommendations to be provided.

In conclusion, while the Mediterranean Diet remains a cornerstone of non-pharmacological treatment for various metabolic diseases, including diabetes mellitus, its impact on glycemic control in insulin-treated patients with T2D appears limited. However, the findings from this survey show a general deviation from the dietary indications according to national guidelines, suggesting that more time should be devoted to proper education of patients regarding the consumption of certain foods (for example, emphasizing the importance of increasing fruit consumption) with a particular focus on alcohol consumption, which was strongly related to the risk of hypoglycemia even for minimal amounts.

CRediT authorship contribution statement

Caterina Formichi: Writing – original draft, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Sonia Caprio:** Writing – original draft, Methodology, Investigation, Formal analysis, Data curation. **Stefano Auddino:** Formal analysis. **Felicia Rizza:** Investigation. **Barbara Paolini:** Writing – review & editing, Supervision. **Laura Nigi:** Investigation, Data curation. **Francesco Dotta:** Writing – review & editing, Supervision, Funding acquisition.

Declaration of competing interest

The authors declare no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.hnm.2025.200330.

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