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ORIGINAL RESEARCH

Glycemic variability in relation to the oral disposition index in subjects with different stages of glucose tolerance - Review of the evidence

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1. ABSTRACT

The analyzed study evaluated 220 adults with normal glucose regulation, impaired glucose metabolism, or newly diagnosed type 2 diabetes. Using an oral glucose tolerance test and 72-hour continuous glucose monitoring, the authors observed that mean glycemia and numerous indices of variability increased progressively along the metabolic continuum, while the oral disposition index decreased. All variability indices considered were inversely correlated with this integrated indicator of pancreatic beta-cell function.The publication contributes to the narrative of “The Choice to Live in Health or Illness” by Dr. A. Colonnese and R. Panzironi, according to which increasing glycemic instability accompanies the worsening of the pancreas's ability to compensate for insulin resistance. Independent studies confirm that glycemic oscillations increase even in impaired glucose regulation and that a poorer post-meal beta-cell response is associated with a higher MAGE. A recent meta-analysis supports the general picture but emphasizes that much of the evidence is observational. The relationship is therefore well-documented as a pathophysiological association, without proving that glycemic oscillations alone are the cause of beta-cell damage.

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MISSION

LIFE Science Hub – Journal of Science was founded with the aim of making scientific knowledge accessible without giving up methodological rigour, quality of sources and authoritativeness of content. The journal promotes the dissemination of knowledge in the health, nutrition, medical and longevity sciences, building a bridge between the world of research and society.

Through articles, reviews, in-depth analyses and expert contributions, the Journal champions evidence-based medicine and science, fostering a correct interpretation of scientific data and countering misinformation. Every piece of content is developed with the aim of translating the complexity of research into understandable, useful and applicable information, while keeping intact the principles of accuracy, transparency and scientific independence.

Free from political, industrial and commercial influence, the journal stands as an authoritative and independent editorial space, dedicated to promoting scientific culture, professional development and the growth of health awareness among the public.

2. ANALYZED STUDY

The research question was whether glycemic instability, detected during daily life with continuous monitoring, changes along the progression from normal glucose tolerance to type 2 diabetes and whether it is linked to pancreatic beta-cell function. Beta cells are the cells in the pancreas that produce insulin, the hormone that helps keep blood glucose within limits compatible with the proper functioning of the body.The authors' hypothesis was that a reduced ability of the pancreas to adequately increase insulin secretion when tissues become less sensitive to insulin would be accompanied by wider glycemic oscillations. To estimate this compensatory capacity, they used the oral disposition index, obtained by multiplying an early insulin secretion index by an insulin sensitivity index. A lower value indicates that the insulin response does not sufficiently compensate for insulin resistance.The study is relevant to sections 3.1 and 14.5 of "The Choice to Live in Health or Illness" by Dr. A. Colonnese and R. Panzironi because it documents the segment of the narrative that links the deterioration of beta-cell function to greater glycemic instability. Since the design is cross-sectional, meaning it is based on measurements collected in a single period, it can show associations between variables but cannot establish which phenomenon comes first nor demonstrate a cause-effect relationship.

3. MATERIALS AND METHODS OF THE ORIGINAL STUDY

The study recruited 220 subjects between January 2012 and January 2013. Participants were divided into four groups: 47 with normal glucose regulation, 52 with impaired glucose metabolism, 61 with diabetes identified solely by the two-hour plasma glucose value from an oral glucose tolerance test, and 60 with newly diagnosed diabetes defined by elevated fasting and two-hour glycemia. The group with impaired metabolism included 8 people with impaired fasting glucose, 18 with impaired glucose tolerance, and 26 with both conditions.Subjects with acute complications, disorders capable of altering glucose metabolism, or previous treatment with antidiabetic drugs were excluded. All participants underwent an oral glucose tolerance test with 75 grams of glucose. Glycemia and insulin were measured at 0, 30, 60, 90, and 120 minutes. From these measurements, the authors calculated the Matsuda insulin sensitivity index, the early insulinogenic index ΔI30/ΔG30, and their product, the oral disposition index.After the test, each participant wore a continuous glucose monitoring system for 72 hours. The analyses used data from the first and second full days. During the monitoring period, standardized meals were provided, equal to 30 kcal per kilogram of body weight per day, with 50% of calories from carbohydrates, 15% from protein, and 35% from fat. The authors calculated the standard deviation of glycemia, mean glycemia, the hyperglycemia risk index, CONGA1, MODD, and MAGE. MAGE measures the amplitude of the most significant glycemic oscillations; MODD, on the other hand, measures how much profiles differ between consecutive days.Comparisons between groups were performed using analysis of variance. Correlations between variability indices and the oral disposition index were examined using the Pearson test. The authors report that the main associations remained significant after adjustment for age, sex, body mass index, blood pressure, lipids, and glycated hemoglobin. The coefficients of the adjusted analyses are not reported in the available material.

4. RESULTS

The most immediate result is that, in transitioning from normal glucose regulation to newly diagnosed diabetes, glycemia became, on average, higher and more unstable. Mean glycemia increased from 5.9 ± 0.5 mmol/L in the normoglycemic group to 6.7 ± 0.7 mmol/L in the group with impaired metabolism, 7.7 ± 1.0 mmol/L in the group with diabetes identified at two hours, and 8.7 ± 1.5 mmol/L in overt diabetes. All overall differences between groups were statistically significant.Indices describing fluctuations also increased progressively. The standard deviation of glycemia, which expresses how far values deviate from the mean, rose from 0.9 ± 0.3 to 2.2 ± 0.6 mmol/L. MAGE increased from 2.1 ± 0.6 to 4.8 ± 1.6 mmol/L. MODD grew from 0.9 ± 0.3 to 2.1 ± 0.7 mmol/L. CONGA1, which estimates glycemic differences one hour apart, increased from 1.0 ± 0.2 to 1.8 ± 0.4 mmol/L. The hyperglycemia risk index also increased, with a median rising from 0.8 to 6.4.In parallel, the compensatory capacity of beta cells decreased. The oral disposition index was 745, with an interquartile

range of 546-947, in the group with normal glucose regulation; it fell to 362 in those with impaired metabolism, to 203 in those with diabetes identified at two hours, and to 91 in those with diabetes defined by elevated fasting and two-hour glycemia. The progressive reduction was statistically significant.Across all 220 participants, all glycemic indices were inversely associated with the oral disposition index: as the index decreased, glycemic instability or the mean level of glycemia increased. The correlations were r = –0.66 for standard deviation and mean glycemia, 0.72 for the hyperglycemia risk index, 0.59 for CONGA1, 0.61 for MODD, and r = –0.65 for MAGE; for all, P < 0.001. A negative coefficient indicates that the two variables move in opposite directions, but it does not prove that one causes the other.

5. INTERPRETATION

In simple terms, the data indicate that less stable glycemia tends to occur when the pancreas is less effective at compensating for the reduced tissue response to insulin. This result is consistent with the fact that, after a meal, an insufficient early insulin response can leave glucose in the blood for longer and promote higher spikes.The segment specifically documented by the publication subject to the Evidence Review is: lower beta-cell function integrated with insulin sensitivity greater glycemic variability and higher mean glycemia. The oral disposition index does not directly measure all pancreatic functions; it is an indicator derived from the oral glucose tolerance test and can also be influenced by gut hormones and the clearance of insulin by the liver, as acknowledged by the authors themselves.The study does not demonstrate that beta-cell loss is the sole driver of glycemic instability. Diet, physical activity, sleep, stress, medications, and the liver's ability to produce glucose can all modify the glycemic profile. However, the use of standardized meals and the inclusion of individuals not treated with antidiabetic drugs reduce some major sources of variability. The main interpretative caution remains the cross-sectional design: the observed relationship is strong and consistent, but it does not allow for the establishment of an individual causal sequence.

6. INDEPENDENT SUPPORTING EVIDENCE

Independent confirmation of the progression of glycemic oscillations along the metabolic continuum comes from a cross-sectional study of 162 people: 53 with normal glucose tolerance, 53 with impaired glucose regulation, and 56 with newly diagnosed, untreated type 2 diabetes. After three days of continuous monitoring, the groups with impaired regulation and diabetes showed significantly higher standard deviation, mean amplitude of glycemic excursions, and MAGE compared to the normoglycemic group. In those with diabetes, day-to-day variability, post-meal excursions, and nocturnal glycemia were also higher. This study directly confirms the book's statement that oscillations become wider even before overt diabetes; however, as it is cross-sectional, it does not establish the causal role of beta-cell function [1].A second independent study evaluated the link with the pancreas more closely. In 59 people with type 2 diabetes, monitored for three days with CGM and subjected to a mixed-meal test, poorer postprandial beta-cell function was the primary determinant of a higher MAGE. Postprandial beta-cell function is the pancreas's ability to modulate insulin secretion in response to food. The authors also considered insulin sensitivity, glycated hemoglobin, body mass index, age, duration of diabetes, carbohydrate intake, and therapy; in their model, these factors explained MAGE variability less than the beta-cell response did. The result is particularly relevant to the book's narrative, but it concerns patients who are already diabetic, predominantly treated or previously treated, and does not demonstrate the entire natural history of the disease [2].A systematic review with meta-analysis published in 2024 included 71 studies conducted on people without diabetes, evaluated with continuous monitoring for at least 24 hours. The synthesis found that multiple measures of glycemic variability are higher in prediabetes compared to normal glucose regulation and that variability appears inversely associated with beta-cell function. However, the authors highlighted that the majority of the included studies were cross-sectional and that associations with insulin sensitivity, adiposity, hepatic steatosis, lipids, and blood pressure were unclear. This evidence expands and contextualizes the result of the analyzed study: it supports the general consistency of the link

but requires prospective studies to define the direction and causal independence of the association [3].

7. CONFLICTING EVIDENCE

No directly conflicting evidence of sufficient relevance has been identified; this does not prove the absence of contrary findings. The main element of caution stems from the largest available systematic review: glycemic variability appears to be inversely associated with beta-cell function, but the relationship with insulin sensitivity and many other cardiometabolic factors remains unclear. Furthermore, the majority of available studies were cross-sectional, meaning it is not possible to determine with certainty whether reduced beta-cell function precedes glycemic instability, results from it, or if both reflect other common metabolic processes [3].Generalizability also requires caution because the studies used non-identical populations, monitoring durations, dietary regimens, and mathematical indices. The most balanced interpretation is therefore that the loss of beta-cell compensatory capacity is an important correlate of increased glycemic variability, not the only possible explanation for every fluctuation observed in daily life.

8. QUADRO COMPARATIVO E SINTESI DELLE EVIDENZE

The table distinguishes the publication subject to the Evidence Review from the independent research used to confirm the book's specific narrative.

Quadro comparativo

Reference	Study type	Population or model	Main result	Direction of evidence	Strength of evidence
Original study	Cross-sectional study with continuous monitoring	220 adults ranging from normal glucose regulation to newly diagnosed diabetes	Variability indices increased and the oral disposition index decreased progressively; inverse correlations between all indices and the oral index.	direct confirmation	moderate
[1]	Cross-sectional observational study	162 adults: normal tolerance, impaired glucose regulation, and newly diagnosed type 2 diabetes	Standard deviation, mean amplitude of glycemic excursions, and MAGE were higher in impaired glucose regulation and diabetes compared to normal tolerance.	direct confirmation	moderate
[2]	Cross-sectional observational study	59 people with type 2 diabetes monitored for three days	Worse postprandial beta-cell function was the main determinant of a higher MAGE.	direct confirmation	moderate
[3]	Systematic review and meta-analysis	71 studies in people without diabetes using continuous glucose monitoring	Glycemic variability was higher in prediabetes and appeared inversely associated with beta-cell function.	indirect confirmation	moderate

9. SINTESI EDITORIALE E CONCLUSIONI

CONCLUSIONS

The study analyzed shows that the increase in glycemic variability runs parallel to the reduction of the oral disposition index across different stages of glucose tolerance. Its function in the book is therefore scientifically precise: to document the association between lower compensatory capacity of beta cells and greater instability of glycemia.

Independent evidence makes this narrative quite well-supported. The progression of oscillations from normal metabolism to prediabetes and diabetes has been observed in other samples, while the link with beta-cell function is supported by clinical-observational data and a systematic review. It remains necessary to validate through prospective studies whether glycemic variability represents primarily an early signal, a consequence, or even a factor contributing to beta-cell deterioration.

Aggiornato al 17/11/2026. Questo contenuto riflette una sintesi divulgativa delle evidenze scientifiche al momento della pubblicazione e non sostituisce il parere medico.

10. TRANSPARENCY AND SCIENTIFIC RESPONSIBILITY

Artificial Intelligence was used solely as a tool for editorial and documentary support. All content, interpretations, bibliographic citations and conclusions have been verified, reviewed and approved by the author, who assumes full scientific responsibility for them.

The manuscript was also subjected to independent peer review prior to publication.

To ensure the greatest transparency, the complete history of the article, including the dates of submission, revision, acceptance and publication, as well as information on the peer review process, is available on the dedicated Article History page.

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