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ORIGINAL RESEARCH

Predictive performance of glycated hemoglobin for incident diabetes compared to the glucose tolerance test according to central obesity - Evidence review

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1. ABSTRACT

The analyzed study compared, in 7,512 Korean adults without diabetes followed for up to 12 years, the ability of glycated hemoglobin (HbA1c, an indicator of average glucose exposure over the previous months) and blood glucose measured two hours after an oral glucose load to predict the development of diabetes. In the overall population, impaired glucose tolerance identified by the load test was associated with a higher future risk compared to isolated elevated HbA1c. In people with abdominal obesity, however, the predictive differences between the two criteria became less clear.The research contributes to the passage from “The Choice to Live in Health or Illness” by Dr. A. Colonnese and R. Panzironi, according to which HbA1c and the load test do not necessarily identify the same subjects and do not describe identical aspects of glucose metabolism. Independent studies confirm often limited concordance between the tests and differences in the identified metabolic profiles. Results remain non-uniform regarding how obesity modifies diagnostic agreement. The most prudent conclusion is that the tests are complementary, not interchangeable in every person.

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MISSION

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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 HbA1c could identify people at high risk for diabetes with efficacy comparable to blood glucose measured two hours after an oral glucose tolerance test (OGTT, a test that evaluates how the body handles a standardized amount of glucose). The authors also verified whether the presence of central obesity, defined by waist circumference, modified this comparison.The hypothesis was that HbA1c and OGTT did not have the same prognostic significance in all participants. The issue is relevant because HbA1c requires a single blood draw and no fasting, whereas the OGTT requires preparation, the intake of 75 grams of glucose, and multiple blood draws. However, the greater convenience of HbA1c does not, by itself, prove that it selects the same population identified by the OGTT.The relevance to the section "The Choice to Live in Health or Illness" by Dr. A. Colonnese and R. Panzironi is precise: the study documents that HbA1c and post-load blood glucose can classify different people and that their predictive value changes in relation to abdominal obesity. It does not, however, demonstrate that one test should replace the other in individual clinical practice, nor does it establish a causal relationship between a single glycemic value and the subsequent development of diabetes.

3. MATERIALS AND METHODS OF THE ORIGINAL STUDY

A prospective population cohort from the Korean Genome and Epidemiology Study, consisting of residents from two Korean communities—one urban and one rural—was analyzed. At baseline, between 2001 and 2002, volunteers aged 40 to 69 were recruited. After exclusions, including previously known or baseline-detected diabetes, anemia, and hematological conditions potentially capable of altering HbA1c, 7,512 participants remained, 3,536 of whom were men.Every two years until 2014, both HbA1c and OGTT were performed. Prediabetes based on the glucose tolerance test corresponded to a two-hour glycemia between 140 and 199 mg/dL; elevated HbA1c corresponded to values from 5.7% to 6.4%. Participants were divided into four groups: both tests normal; elevated HbA1c with normal glucose tolerance; impaired tolerance with normal HbA1c; and both tests impaired.Central obesity was defined as a waist circumference of 90 cm or greater in men and 85 cm or greater in women. The outcome was incident diabetes, identified through a new clinical diagnosis or fasting glycemia of 126 mg/dL or greater, two-hour glycemia of 200 mg/dL or greater, or HbA1c of 6.5% or greater.To estimate the association with future diabetes, the Cox model was used, an analysis that compares the rate at which an event occurs over time across different groups. The result is expressed as a hazard ratio or HR: an HR greater than 1 indicates that the event occurred more frequently compared to the reference group. The models were adjusted for demographic, renal, inflammatory, metabolic, blood pressure, and socioeconomic variables. The ability to distinguish who would develop diabetes was also evaluated using the C-index, an index ranging between 0.5 and 1, where higher values indicate better discrimination.

4. RESULTS

At the beginning of the study, the average age was 51.6 years and the average body mass index was 24.5 kg/m². The four groups included 4,058 people with both parameters normal, 1,886 with only elevated HbA1c, 692 with only impaired glucose tolerance, and 876 with both abnormalities. The group with both tests altered showed, on average, higher values of blood pressure, triglycerides, and HOMA-IR index, an indirect estimate of insulin resistance.During a median follow-up of 11.5 years, 1,341 participants developed diabetes, equal to 17.6% of the cohort and 22.1 new cases per 1,000 person-years. The cumulative frequency was 8.4% in the group with both tests normal, 22.2% with only elevated HbA1c, 32.7% with only impaired glucose tolerance, and 59.9% when both measures were altered.Compared to the group with normal results, isolated elevated HbA1c was associated with a higher rate of diabetes onset: adjusted HR 2.79; 95% confidence interval from 2.40 to 3.26. Isolated impaired glucose tolerance was associated with an even greater increase: HR 4.29; 95% confidence interval from 3.56 to 5.17. When both tests were altered, the association was more marked: HR 9.94; 95% confidence interval from 8.53 to 11.59. These data show a prognostic gradient, but do not prove that the test causes diabetes: the tests detect different manifestations of an already present metabolic

vulnerability.In the overall population, adding the two-hour blood glucose to fasting blood glucose produced a C-index of 0.79, higher than the value of 0.75 obtained by adding HbA1c. In people without central obesity, the advantage of the OGTT remained visible: 0.79 versus 0.75. In people with central obesity, however, the models with HbA1c and post-load blood glucose both reached a C-index of 0.75. The risks associated with isolated impaired tolerance and isolated elevated HbA1c also became closer, while remaining numerically higher in the first group: HR 3.95 versus 2.82.The sensitivity of HbA1c for identifying impaired glucose tolerance defined by the OGTT was 55.9% in the entire cohort. It was higher in people with central obesity, 59.1%, compared to people without central obesity, 49.4%. The positive predictive value was also higher in the group with central obesity, 35.1% versus 29.8%. This means that, in this sample, an HbA1c in the prediabetes range coincided more often with an alteration in the OGTT in people with a larger waist circumference; it does not mean that HbA1c identifies all cases detectable with the OGTT.

5. INTERPRETATION

In simple terms, HbA1c and OGTT look at glucose metabolism from two different perspectives. HbA1c summarizes the average exposure of red blood cells to glucose over weeks or months. The two-hour post-load glycemia, on the other hand, describes the body's response to a standardized metabolic challenge. This is why two people may have a normal result in one test and an abnormal one in the other.The segment directly supported by the study is as follows: HbA1c and post-load glycemia do not necessarily identify the same individuals at risk, and their ability to predict diabetes varies based on the presence of abdominal obesity. In the Korean cohort, the OGTT had superior predictive capacity in the general population and especially in people without central obesity. In people with central obesity, the difference between the two tests was reduced.The authors suggest that the greater concordance observed in central obesity may depend on metabolic characteristics specific to this condition. This is a plausible interpretation, not a causal demonstration. The study did not directly measure all the mechanisms linking visceral adiposity, insulin resistance, insulin secretion, and hemoglobin glycation. Furthermore, the cohort included Korean adults aged 40-69; the results cannot be automatically transferred to all ages, geographical origins, or clinical conditions.

6. INDEPENDENT SUPPORTING EVIDENCE

A large U.S. analysis of 7,412 adults selected from the NHANES program compared OGTT, HbA1c, and fasting glycemia in people without a known diagnosis of diabetes. When the OGTT indicated diabetes, HbA1c agreed in 34.1% of cases; when the OGTT indicated prediabetes, the agreement with HbA1c was 46.1%. The study is cross-sectional, so it does not measure the progression toward diabetes, but it directly confirms the book's premise that no single test fully describes the same metabolic population as another [1].The IRAS study examined 855 participants of diverse ethnic backgrounds using OGTT, HbA1c, and more in-depth measures of insulin sensitivity and insulin secretion. In the subgroup of 385 people considered at high risk, HbA1c between 5.7% and 6.4% identified 23.6%, while impaired fasting glycemia and impaired glucose tolerance detected 69.1% and 59.5%, respectively. Furthermore, two-hour blood glucose showed stronger correlations with insulin sensitivity and triglycerides compared to HbA1c. These results support the idea that the criteria are not equivalent and may reflect different pathophysiological profiles [2].In 949 outpatients with overweight or obesity, HbA1c classified more people as prediabetic than the OGTT: 42% versus 22% in men and 40% versus 18% in women. The overall agreement between the tests was only 60%. People identified by the OGTT showed higher post-load insulin values and HOMA index compared to those who were positive only for HbA1c. This research is also cross-sectional, but it reinforces the narrative regarding obesity: in this population, the two tests can identify groups with different metabolic characteristics, not simply two versions of the same phenomenon [3].Taken together, these independent findings do not establish which test is always superior. However, they convergently show that HbA1c, fasting glycemia, and OGTT are not perfectly interchangeable tools. The original study adds an important longitudinal element: the classification differences also have consequences for predicting diabetes in subsequent years.

7. CONFLICTING EVIDENCE

A Chinese cross-sectional study of 4,325 adults without known diabetes found that the agreement between HbA1c and OGTT decreased as the body mass index increased: the kappa coefficient, a measure of agreement beyond that attributable to chance, was 0.359 in normal-weight individuals, 0.312 in those who were overweight, and 0.275 in those with obesity. Using HbA1c thresholds adjusted for weight category improved agreement in obesity, but it remained below 0.4 [4].This result does not negate the original study, which observed a greater similarity in the prognostic capacity of the two tests among people with central obesity. However, it highlights that diagnostic concordance at baseline and the ability to predict future diabetes are not the same thing. Furthermore, obesity can be defined by waist circumference or body mass index, and these measures do not identify exactly the same individuals. The direction of the effect of obesity on the agreement between tests therefore appears to be dependent on the population, the threshold used, and the outcome examined.

8. QUADRO COMPARATIVO E SINTESI DELLE EVIDENZE

The table distinguishes the publication reviewed from the independent research used to verify the narrative in the book's paragraph.

Quadro comparativo

Reference	Study type	Population or model	Main result	Direction of evidence	Strength of evidence
Original study	Prospective cohort	7,512 Korean adults without diabetes, aged 40-69	OGTT more predictive than HbA1c in the general population; similar performance in central obesity.	direct confirmation	moderate
[1]	Cross-sectional observational	7,412 US NHANES adults	Limited agreement between OGTT, HbA1c, and fasting glycemia for diabetes and prediabetes.	direct confirmation	moderate
[2]	Observational	855 IRAS participants; 385 high-risk	HbA1c, fasting glycemia, and two-hour glycemia identified groups with different metabolic profiles.	indirect confirmation	moderate
[3]	Cross-sectional observational	949 patients with overweight or obesity	HbA1c and OGTT showed limited agreement and selected different metabolic phenotypes.	biologically consistent evidence	moderate
[4]	Cross-sectional observational	4,325 Chinese adults without known diabetes	HbA1c-OGTT diagnostic agreement decreased as body mass index increased.	discordant evidence	moderate

9. SINTESI EDITORIALE E CONCLUSIONI

CONCLUSIONS

The analyzed study convincingly argues that elevated HbA1c and impaired post-load glycemia are not overlapping indicators of metabolic risk. In the general population of the Korean cohort, the OGTT was a better predictor of future diabetes; in cases of abdominal obesity, this predictive difference diminished. Independent evidence confirms that these tests often identify different individuals and metabolic profiles. Their complementarity is therefore well-supported, while the generalization of the effect of obesity requires validation in other populations and with standardized definitions of adiposity.

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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