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ORIGINAL RESEARCH

Is the current definition of diabetes relevant to the risk of all-cause, cardiovascular, and non-cardiovascular mortality? - Evidence review

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ONLINE ARTICLE

ARTICLE INFORMATION

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1. ABSTRACT

The original study analyzed 29,714 European adults to assess whether fasting glycemia and glycemia measured two hours after an oral glucose load were associated with total, cardiovascular, and non-cardiovascular mortality. After approximately eleven years of follow-up, elevated glycemic values were associated with higher mortality. For cardiovascular mortality, the increase in risk in relation to post-load glycemia appeared progressive, without a sudden threshold.In section 2.4.1 of “The Choice to Live in Health or Illness” by Dr. A. Colonnese and R. Panzironi, this research contributes to the narrative that post-load glycemia can identify individuals with increased cardiovascular risk who would not be fully identified by fasting glycemia alone. Independent cohorts support the association between elevated post-load glycemia, cardiovascular events, and mortality, but not all confirm a clear predictive superiority over fasting glycemia. The evidence is therefore consistent with a prognostic role for post-load glycemia, without demonstrating that it directly describes cardiovascular damage or that its treatment necessarily reduces events.

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 fasting glycemia and glycemia measured two hours after an oral glucose tolerance test were associated with the risk of death, and whether this relationship followed a clear threshold or a gradual trend. The oral glucose tolerance test, or OGTT (a test in which the body's management of a standard amount of glucose is measured), can reveal an increase in glycemia after a meal that is not always visible while fasting.The relevance to paragraph 2.4.1 is specific: the publication examines whether post-load measurement identifies a risk of cardiovascular mortality across the entire glycemic range and not just beyond the diagnostic threshold for diabetes. In "The Choice to Live in Health or Illness" by Dr. A. Colonnese and R. Panzironi, the study is used to argue that post-load glycemia can signal at-risk individuals more effectively than fasting glycemia alone.As a prospective observational study, the research can show that higher glycemic levels more frequently precede death in the observed groups. However, it cannot prove that an increase in post-load glycemia directly causes cardiovascular damage, nor can it establish that reducing that value prevents clinical events.

3. MATERIALS AND METHODS OF THE ORIGINAL STUDY

DECODE was a prospective collaboration of 22 European cohorts. The analysis included 29,714 people aged between 30 and 89, with baseline glycemic measurements. The total observation period was approximately eleven years, for 329,050 person-years: this measure sums the participation time of all subjects followed.The authors evaluated fasting plasma glucose and plasma glucose two hours after an oral glucose tolerance test. The outcomes were all-cause mortality, cardiovascular mortality, and non-cardiovascular mortality. To estimate risk differences, they used Cox regression models, an analysis that compares the rate at which an event occurs over time across the studied groups. The result is expressed as a hazard ratio or HR: an HR greater than 1 indicates a higher frequency of the event compared to the reference group.The detailed inclusion and exclusion criteria for the individual cohorts, the exact enrollment period, the clinical characteristics of the participants, the distribution by sex, the glucose dosages used in the oral test, and the methods for ascertaining causes of death are not reported in the available material, which consists only of the abstract.

4. RESULTS

The main finding is that both high and very low glycemic values were associated with increased mortality, overall forming a J-shaped relationship. In practice, the risk was not at its minimum at the extremes of the glycemic distribution. However, this trend does not equate to proof that low glucose levels cause mortality: they could reflect comorbidities, frailty, or other factors not reported in the abstract.Compared to fasting glycemia between 4.50 and 6.09 mmol/L, fasting glycemia equal to or greater than 7.0 mmol/L was associated with an adjusted HR of 1.6 for all-cause mortality, 1.6 for cardiovascular mortality, and 1.6 for non-cardiovascular mortality. This corresponds to a higher rate of death in groups with fasting glycemia in the diagnostic range for diabetes compared to the reference group.For post-load glycemia, the comparison with the group between 4.51 and 5.50 mmol/L showed that diabetes defined by glycemia two hours after the load equal to or greater than 11.1 mmol/L was associated with an HR of 2.0 for all-cause mortality, 1.9 for cardiovascular mortality, and 2.1 for non-cardiovascular mortality. These values indicate an approximately double risk compared to the reference. Very low post-load glycemia, between 3.01 and 4.50 mmol/L, was associated with an HR of 1.1 for all-cause mortality, 1.1 for cardiovascular mortality, and 1.1 for non-cardiovascular mortality; the estimates were small, and some confidence intervals included the value of no difference.An element directly relevant to the book is that subjects with diabetes not previously recognized via post-load glycemia had a risk of death not significantly different from that of people with already known diabetes. This risk was, however, significantly higher than that observed in diabetes undiagnosed by the fasting glycemia criterion alone. Furthermore, post-load values between 10.01 and 11.09 mmol/L were associated with mortality similar to that of subjects classified as diabetic via fasting glycemia equal to or greater than 7.0 mmol/L.According to the

authors, for cardiovascular mortality, the relationship with post-load glycemia was gradual and increasing, without an evident threshold. The abstract does not report detailed numerical values for each step of the relationship, nor formal statistics directly comparing the predictive accuracy of the two tests.

5. INTERPRETATION

In simple terms, a person may have a fasting glycemia that is not clearly diabetic but show a significant increase in glycemia after a glucose load. The study suggests that this condition is not necessarily harmless from a prognostic standpoint. The segment of the book's narrative documented by the publication is therefore: higher post-load glycemia greater observed cardiovascular mortality possible identification of at-risk individuals whom fasting glycemia alone may not classify as diabetic.The result is biologically plausible because post-load glycemia reflects the body's ability to control glucose when it rises after carbohydrate intake. A high value can be an indicator of reduced insulin sensitivity or an insufficient insulin response. However, these metabolic alterations were not measured directly in the available material and cannot be attributed as the cause of the deaths.The statement in the book that cardiovascular damage may develop long before overt diabetes requires caution. The study demonstrates a prognostic association, does not directly measure early vascular lesions, and does not prove a causal sequence from the glycemic peak to cardiovascular damage. Furthermore, although the results indicate that the post-load test identified people at high risk, the abstract does not report a formal statistical comparison of the overall predictive capacity between OGTT and fasting glycemia.

6. INDEPENDENT SUPPORTING EVIDENCE

A confirmation particularly close to the book's narrative comes from the Cardiovascular Health Study. In 4,014 U.S. adults aged 65 or older, without treated diabetes or a history of heart attack or stroke, 764 cardiovascular events were recorded over 8.5 years. Glycemia two hours after a glucose load showed a linear relationship with the risk of cardiovascular events: for every 10 mg/dL increase, the HR was 1.02. When fasting glycemia and post-load glycemia were considered together, only post-load glycemia remained associated with events. This study directly confirms the passage stating that the post-load measurement can offer additional prognostic information compared to the fasting value alone, at least in the elderly. The main limitation is the advanced age of the population, which does not allow for the automatic transfer of this estimate to younger people [1].An additional cohort, obtained by combining three population studies in Mauritius, Fiji, and Nauru, followed 9,179 people for a period ranging from five to twelve years. In men with isolated post-load hyperglycemia—that is, post-load glycemia equal to or greater than 11.1 mmol/L but fasting glycemia less than 7.0 mmol/L—total mortality was higher compared to people without diabetes; in women, the HR was 2.0. Cardiovascular mortality was also higher, with an HR of 2.3 in men and 2.6 in women. This result supports the concept that an alteration detectable only with the post-load test can identify people with an unfavorable prognosis. It remains an observational study and does not establish which biological mechanism explains the increase in mortality [2].In the U.S. national NHANES II sample, 3,092 adults between 30 and 74 years of age who underwent an OGTT were followed until 1992. People with isolated post-load hyperglycemia had higher total mortality compared to normoglycemic subjects, with a relative risk adjusted for age and sex of 1.6. In the fully adjusted analysis, both fasting glycemia and post-load glycemia were associated with mortality with very similar estimates. The data confirms that post-load hyperglycemia is a prognostic signal independent of various cardiovascular factors, but it tempers the idea of a constant superiority of the post-load test in every population [3].

7. CONFLICTING EVIDENCE

Evidence is not uniform regarding the greater efficacy of post-load glycemia compared to fasting glycemia. In the Chin-Shan Community Cardiovascular Cohort in Taiwan, 2,165 adults were followed for 10.5 years, during which 166 major cardiovascular events occurred. The highest quartile of fasting glycemia was associated with an increased cardiovascular risk, with a relative risk of 1.74 compared to the lowest quartile; for post-load glycemia, the increase was 2.05. However, the two measures had the same discriminative capacity reported by the authors, and in reciprocal models, both remained associated with

cardiovascular events. This result does not negate the prognostic value of post-load glycemia, but it does not confirm a clear superiority over the fasting value [4].The discrepancy may depend on age, geographic origin, the frequency of glycemic abnormalities, the number of events, diagnostic criteria, and the way risk prediction is assessed. No sufficiently relevant directly conflicting evidence has been identified that demonstrates an inverse association between elevated post-load glycemia and cardiovascular risk; this does not prove the absence of contrary results.

8. QUADRO COMPARATIVO E SINTESI DELLE EVIDENZE

The table distinguishes the study under review from the independent publications used to confirm or define the narrative of the book's paragraph.

Quadro comparativo

Reference	Study type	Population or model	Main result	Direction of evidence	Strength of evidence
Original study	Prospective cohort collaboration	29,714 European adults, 22 cohorts, 11 years	Elevated post-load glycemia was associated with higher mortality; for cardiovascular mortality, the relationship was graded and increasing.	direct confirmation	moderate
[1]	Prospective observational	4,014 US adults aged 65 or older	In the model including both measurements, only post-load glycemia remained predictive of cardiovascular events.	direct confirmation	moderate
[2]	Prospective observational	9,179 adults in Mauritius, Fiji, and Nauru	Isolated post-load hyperglycemia was associated with higher total and cardiovascular mortality.	indirect confirmation	moderate
[3]	Prospective observational	3,092 US adults from the NHANES II sample	Isolated post-load hyperglycemia was associated with higher mortality; the prognostic value was similar to that of fasting glycemia.	biologically consistent evidence	moderate

[4]	Prospective observational	2,165 Taiwanese adults	Fasting and post-load glycemia were both associated with higher cardiovascular risk, with similar discriminative capacity.	discordant evidence	moderate

9. SINTESI EDITORIALE E CONCLUSIONI

CONCLUSIONS

The study analyzed clearly supports that glycemia measured two hours after an oral glucose load is associated with mortality, including cardiovascular mortality, and that for the latter, the risk increases progressively without a clear, distinct threshold. Independent evidence confirms that post-load hyperglycemia can identify individuals with a less favorable cardiovascular prognosis even when fasting glycemia is not in the diabetic range. Its greater efficacy compared to fasting glycemia alone is moderately supported, but it is not consistent across all cohorts. The link with cardiovascular risk is therefore well-founded on an observational level, while the causal mechanism and the utility of targeted interventions require further validation.

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.

11. RIFERIMENTI BIBLIOGRAFICI

[1] **Fasting and 2-Hour Postchallenge Serum Glucose Measures and Risk of Incident Cardiovascular Events in the Elderly**
Smith et al., 2002
Archives of Internal Medicine
DOI: https://doi.org/10.1001/archinte.162.2.209

[2] **Isolated post-challenge hyperglycaemia confirmed as a risk factor for mortality**
Shaw et al., 1999
Diabetologia
DOI: https://doi.org/10.1007/s001250051269

[3] **Postchallenge Hyperglycemia and Mortality in a National Sample of U.S. Adults**
Saydah et al., 2001
Diabetes Care
DOI: https://doi.org/10.2337/diacare.24.8.1397

[4] **Fasting and postchallenge hyperglycemia and risk of cardiovascular disease in Chinese: The Chin-Shan Community Cardiovascular Cohort study**
Chien et al., 2008
American Heart Journal
DOI: https://doi.org/10.1016/j.ahj.2008.06.019