Letter to the Editor: KETO CTA Study

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PII: S2772-963X(25)00281-9

DOI: https://doi.org/10.1016/j.jacadv.2025.101861

Reference: JACADV 101861

To appear in: *JACC: Advances*

Received Date: 25 April 2025

Accepted Date: 2 May 2025

Please cite this article as: López-Moreno M, López-Gil JF, Letter to the Editor: KETO CTA Study, *JACC: Advances* (2025), doi: https://doi.org/10.1016/j.jacadv.2025.101861.

Letter to the Editor: KETO CTA Study

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The recent study by Soto-Mota et al. [1] on plaque progression in lean, metabolically healthy individuals on a ketogenic diet with elevated LDL-c offers timely insights. However, several methodological issues warrant consideration to contextualize the findings and assess their reliability.

Notably, the study preregistered the change in noncalcified plaque volume (ΔNCPV) as its primary outcome, yet this is only briefly shown in Figure 1 without proper description. Instead, the authors emphasize percent atheroma volume (PAV), a secondary endpoint. This shift from the prespecified analysis raises concerns of selective reporting. Additionally, the absence of a comparator group limits attribution of changes to the ketogenic diet.

Comparisons with other cohorts were purely descriptive, often involving very small subgroups (e.g., n = 17), and lacked statistical testing or adjustment for confounders. Such indirect comparisons are difficult to interpret and should be presented with caution.

The validity of the regression models is also questionable. Despite claims of meeting assumptions, variables were reported using medians, suggesting non-normal distributions. Visual inspection of scatter plots shows clustering and no clear linear trends. Robust or nonparametric methods might have been more appropriate, and model diagnostics would improve transparency.

Crucially, Table 2 omits protein and total energy intake—key dietary factors influencing cardiometabolic outcomes. Moreover, models did not adjust for energy intake, BMI, or body composition, potentially leading to residual confounding. Mediation analyses involving diet-related variables would have added clarity.

Although the use of Bayes Factors is a strength, the manuscript lacks a detailed explanation of the interpretive framework, and the joint reporting with p-values is not clearly integrated.

The short follow-up (one year) limits the ability to assess long-term cardiovascular impact. Prior research suggests that 3–6 years may be required to observe meaningful plaque changes [2]. The focus on sensitivity analyses in the central figure, despite discrepancies in reported sample size (n = 56 vs. n = 100), may also mislead readers.

Importantly, the lack of association between ApoB or LDL-c and ΔNCPV in the short term does not negate decades of evidence linking elevated LDL-c with cardiovascular risk [3–5]. These results should be viewed as hypothesis-generating, not practice-changing, especially in such a selective population.

Long-term, controlled studies in broader populations are needed to clarify the cardiovascular effects of ketogenic diets in hyperresponders.

Author Contributions: All authors participated in the writing, review and editing of the manuscript. All the authors have read and agreed to the published version of the manuscript.

Funding: Not applicable.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data availability statement: Not applicable.

Disclosure statement: Nothing to disclose.

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