



Correspondence

Methodological issues regarding “Decline in ankle-brachial index is stronger in poorly than in well controlled diabetes: Results from the Heinz Nixdorf Recall cohort study”


ARTICLE INFO

Keywords:

Epidemiologic methods
 Confounder
 Over-parameterization
 Diabetes

To the Editor,

We read with great interest the recent article by Bernd Kowall et al. [1] published in *Atherosclerosis*. The authors concluded that decline in ankle-brachial index (ABI) was stronger in poorly than well-controlled diabetes. In addition, subjects with newly detected diabetes diagnosed by the new HbA1c criterion ($\geq 6.5\%$) did not show an increased decline in ABI over 10 years.

The aim of this letter is to address some methodological issues in the paper. One of the important points in epidemiologic studies is to select the minimum sample size to provide good power for statistical tests. Low sample size leads the test to be unable to detect significant variables. In their paper, the researchers used 3199 participants from a cohort study names “The Heinz Nixdorf Recall Study” without computing the sample size. Despite the apparently large number of individuals, after categorizing them in different groups of HbA1c and diabetes, models were fitted on the five subgroups, some of which consisted of low sample sizes. For example, in the group with HbA1c ≥ 6.5 and without previously known diabetes in the follow-up of 10 years, there are only 57 participants. The estimated Odds Ratios (ORs) were 0.6 (95% CI: 0.1 to 2.3) and 0.4 (95%I: 0.1 to 1.7) in the adjusted models 1 and 2, respectively. The confidence intervals showed that, despite the considerable ORs, due to the low power of the models, it was not possible to detect significant results. Moreover, to avoid over-parameterization, it would be better to have at least 10 events per variable included in the model. It seems that the authors have used “enter mode” to select variables to enter into the multivariate model and simultaneously entered a large number of variables, which is subject to over-parameterization and power reduction. For example, a model with twelve variables was fitted on groups with 44, 57, and 60 participants.

There are several methods for choosing confounding variables in multivariate models. Selection of variables with higher significance

levels, such as $p < 0.20$ or $p < 0.50$ to include in the model can increase power and reduce bias in the small data sets, multicollinearity is considered as well [2]. Other methods of confounder identification such as directed acyclic graph (DAG) [3] and the new and less-known methods like bootstrap and Bayesian model averaging can also be applied [2]. Finally, it is suggested that the authors apply other methods for model selection to avoid over-parameterization and increasing power.

Conflict of interest

The authors declared they do not have anything to disclose regarding conflict of interest with respect to this manuscript.

References

- [1] K. Bernd, E. Raimund, M. Susanne, L. Nils, K. Knut, S. Andreas, Decline in ankle-brachial index is stronger in poorly than in well controlled diabetes: results from the Heinz Nixdorf Recall cohort study, *Atherosclerosis* 284 (May 2019) 37–43.
- [2] E.W. Steyerberg, *Clinical Prediction Models: a Practical Approach to Development, Validation, and Updating*, Springer Science & Business Media, 2008.
- [3] K.J. Rothman, S. Greenland, T.L. Lash, *Modern Epidemiology*, (2008).

Razieh Bidhendi Yarandi
 Department of Epidemiology and Biostatistics, School of Public Health,
 Tehran University of Medical Sciences, Tehran, Iran
 Reproductive Endocrinology Research Center, Research Institute for
 Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran,
 Iran

Mohammad Hossein Panahi*
 Department of Epidemiology and Biostatistics, School of Public Health,
 Tehran University of Medical Sciences, Tehran, Iran
 E-mail address: mohammadpanahi55@yahoo.com.

DOI of original article: <https://doi.org/10.1016/j.atherosclerosis.2019.02.021>

* Corresponding author.

<https://doi.org/10.1016/j.atherosclerosis.2019.04.216>

Received 21 March 2019; Accepted 10 April 2019

Available online 17 April 2019

0021-9150/ © 2019 Published by Elsevier B.V.