Universiteit Leiden
The Netherlands

Response by Siegerink et al to letter regarding article, "Association Between High-Sensitivity Cardiac Troponin and Risk of Stroke in 96 702 Individuals: A Meta-Analysis"

Siegerink, B.; Broersen, L.H.A.; Scheitz, J.F.

Citation
Siegerink, B., Broersen, L. H. A., & Scheitz, J. F. (2020). Response by Siegerink et al to letter regarding article, "Association Between High-Sensitivity Cardiac Troponin and Risk of Stroke in 96 702 Individuals: A Meta-Analysis", *51*(5), E98-E98. doi:10.1161/STROKEAHA.120.029610

Version:	Publisher's Version
License:	Creative Commons CC BY 4.0 license
Downloaded from:	https://hdl.handle.net/1887/3627253

Note: To cite this publication please use the final published version (if applicable).

Letter to the Editor

Stroke *welcomes Letters to the Editor and will publish them, if suitable, as space permits. Letters must reference a* Stroke *published-ahead-of-print article or an article printed within the past 4 weeks. The maximum length is 750 words including no more than 5 references and 3 authors. Please submit letters typed double-spaced. Letters may be shortened or edited.*

Response by Siegerink et al to Letter Regarding Article, "Association Between High-Sensitivity Cardiac Troponin and Risk of Stroke in 96 702 Individuals: A Meta-Analysis"

In Response:

We have read with interest the letter by Noubiap et al in response to our systematic review and meta-analysis of the relationship between high-sensitivity cardiac troponin and incidence of stroke in different populations.

The main criticism of Noudiap et al can simply be summarized as follows: in the atrial fibrillation subgroup analyses, the cutoffs used are specific to and varied between each included study population and, therefore, pooling the point estimates should not be ideally performed and that a narrative review of these studies would have been preferable.

We agree with the authors that the variation in how cardiac troponin (cTn) is handled in the different studies poses some methodological challenges and directly affects the strength of the conclusions. It is for that reason we have put so much emphasis on the differences in what we call coding of cTn in our tables, statistical analysis plan, and discussion. Additionally, we provide a sub-analysis in which we only include studies with the same high-sensitivity cardiac troponin T coding (ie, dichotomized at 14 ng/L which corresponds to the 99th percentile upper reference limit of the respective assay).[1] This approach worked well for the analyses pertaining the general population, but less so for the atrial fibrillation subgroup, mainly due to much lower number of studies included. Still, we do not agree with the notion that this analysis should not have been performed.

We have preregistered our analysis in the PROSPERO database (International Prospective Register of Systematic Reviews) and predefined a priori to analyze the atrial fibrillation population. Preregistration of meta-analyses has many positive effects, such as preventing duplicate work by different teams. But most importantly, preregistration of research is meant to increase the quality of the work by reducing the researcher *df*, which in its extreme form can lead to undesirable practices like p-hacking and harking.[2] Still, a preregistered plan does not preclude critical thinking, and every planned analysis is only justified if it actually yields useful information. As mentioned by Noubiap et al, this analysis shows a low index of heterogeneity and thus suggests that irrespective of the cutoff used to define low versus high-sensitivity cardiac troponin T, beyond a certain level, high-sensitivity cardiac troponin T is associated with an increased risk of stroke in patients with atrial fibrillation. We agree with this interpretation and see herein an argument that our analyses indeed did provide more information, albeit of limited scope, than a simple narrative exploration of the individual studies would have provided.

Finally, the authors allude to an important general problem seen in articles about cTn in the medical literature. Due to evolution of cTn assays towards increasing sensitivity within the past decades, and due to the availability of different assay manufacturers and characteristics, there is a growing need to follow standardized reporting guidelines on cTn levels.[3] Thus, we would like to advocate that all future studies about cTn, irrespective of the population at hand, at least include the 99th percentile upper reference limit cutoff for the used assay, as it can indeed be considered a universal cutoff to define high cTn.[3] A single cutoff has its limitations, but if combined with other analyses that fit the idiosyncrasies of the respective study population, this approach will at least reduce variation in reporting between studies. We hope that the transition towards open science will lead to more open data sets that can be used for individual patient data meta-analysis that will provide us with the much-needed insight into the relation between high-sensitivity cTn and incident stroke risk in different populations.

Disclosures

None.

Bob Siegerink, PhD
Leonie H.A. Broersen, PhD
Jan F. Scheitz, MD
Center for Stroke Research Berlin (CSB) and Klinik für Neurologie mit Experimenteller Neurologie Charité Universitätsmedizin Berlin Germany

References

1. Broersen LHA, Stengl H, Nolte CH, Westermann D, Endres M, Siegerink B, et al. Association between high-sensitivity cardiac troponin and risk of stroke in 96 702 individuals: a meta-analysis. *Stroke*. 2020;51:1085–1093. doi: 10.1161/STROKEAHA.119.028323
2. Bishop D. Rein in the four horsemen of irreproducibility. *Nature*. 2019;568:435. doi: 10.1038/d41586-019-01307-2
3. Januzzi JL Jr, Mahler SA, Christenson RH, Rymer J, Newby LK, Body R, et al. Recommendations for institutions transitioning to high-sensitivity troponin testing: JACC scientific expert panel. *J Am Coll Cardiol*. 2019;73:1059–1077. doi: 10.1016/j.jacc.2018.12.046

(*Stroke*. 2020;51:e98. DOI: 10.1161/STROKEAHA.120.029610.)
© 2020 American Heart Association, Inc.

Downloaded from http://ahajournals.org by on June 22, 2023