

Peer Review File

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Major Revision

Reviewer A

This is a comprehensive review about the value of the quick carotid scan for the detection of asymptomatic carotid artery disease in order to reduce the burden of stroke and disability conferred by the lack of recognition of asymptomatic carotid stenosis and its consequences.

COMMENT-1. Although the article starts off very well, it loses coherence and its quality drops slightly towards the end. In the beginning, the text is well-referenced, whereas half-way down the Discussion the text resembles less the context of a scientific article. More specifically, the 3 paragraphs on page=13 [from "There have been countless presentations at medical meetings and articles published in medical journals debating which means of management of ACS is preferable, but there have been very few presentations or publications on how to find the silent ACS so that it can be treated. It is suggested that it is far past time to put the emphasis and focus on screening seniors to find the asymptomatic causes of strokes so that they can be managed before-hand and those strokes prevented. This needs to be deleted, as they reflect the authors' personal views and stories, rather than facts. For example, it is impossible to verify the statement "At one meeting, there were 86 presentations on how to manage ACS, but only the author LG's one presentation on how to discover the ACS so it could be managed.". Such anecdotal evidence should be removed.

REPLY-1. The authors appreciate the acknowledgment by the reviewer of the value of the quick carotid scan (QCS) for the rapid detection of asymptomatic carotid stenosis (ACS) so that those seniors with it can be sorted out for a full duplex ultrasound examination, further evaluation, and appropriate management in-order to prevent strokes from the ACS and thus reduce the burden and disability of the persisting annual number of strokes. It was pointed out that the text progressed from largely scientific material to that of opinion. But the paper's primary purpose is to introduce a new means of screening for ACS and then to explain its difference and advantages from the present existing methods. It was also noted that we did mention that in many current presentations and publications the emphasis is on the treatment rather than the discovery of the silent (ACS) so that it can be treated. It was felt by the reviewer that the author's comments in the manuscript that there was an excess number of presentations at scientific meetings debating the best treatment of asymptomatic carotid stenosis rather than on finding a truly practical and accurate means of finding the ACS so it could be treated was simply an opinion that should not be included in the manuscript. But the ease of having existing knowledge or opinions presented rather than the new and unfamiliar is not uncommon. But only by arriving at and making known new knowledge and techniques can there be progress. As an example, it was mentioned by the reviewer that it was impossible to verify that there were 86 presentations at a major meeting on

the management of asymptomatic carotid stenosis, but only one, that of an author of this paper, on finding the silent disease so it could be treated. But that was the case at the 2019 Veith Symposium that that has a unique broadness in paper and subject acceptance, and can be verified by its presence in the Symposium program.

CHANGES IN THE TEXT-1: The impression of the reviewer was that there was too much emphasis in the reviewed paper on the different methods of treating ACS and too little attention to finding and determining the most effective and accurate means of finding the ACS so it could be treated and strokes prevented, and that much of this should be deleted from the paper. But to reduce strokes, it was necessary to point out the on-going emphasis on treating the silent ACS rather than directing more attention to discovering the ACS in the first place so that it could be treated and for which our new screening method, the QCS, was introduced. This is the only means of reducing strokes and is the essence of this paper, we did par down some of the text broadly without removing that essence of the paper. The paper is attempting to introduce a new major breakthrough in Medicine which does require scientific input but also explanation and opinion. We did make some general changes in the attempt to reduce the later without diluting the essence of the message. The most “objectionable” portions of the manuscript in that regard were too general to be pin-pointed by page and line, but some has been deleted as can best be done without removing and changing the purpose of the paper. Without change, there will be no change, and there has been no change or reduction in strokes for decades.

COMMENT 2: There is a lot of personal opinion and information about not really scientific facts, whereas discussion of some relevant articles is missing. For example, don't the authors think that they should mention and discuss the following article: Paraskevas KI, Eckstein HH, Mikhailidis DP, Veith FJ, Spence JD. Rationale for screening selected patients for asymptomatic carotid artery stenosis. *Curr Med Res Opin.* 2020 Mar;36(3):361-365.doi:10.1080/03007995.2020.1713075.Epub 2020 Jan 13.

REPLY 2: There is inclusion of some personal opinion in the paper as well as the reporting of scientific facts. But the paper encompasses both the introduction of a new scientific method for screening that can discover the (ACS) that is the cause of 80% of strokes due to CAD and that is required if we are to significantly reduce strokes as well as pointing out that our focus at this time is more on debating different means of treating the ACS than of finding it so that it could be treated preemptively and strokes prevented. Hence this paper contains both scientific factual material and opinions of goals and comparative methods. We agree with the reviewer that the article with the lead author of Paraskevas has valuable contributions regarding the helpful use of risk factors to select for further studies. The article was received by the authors late, but the authors agree with the reviewer that the article should have been included and was so added.

CHANGES IN THE TEXT 2: The authors did attempt to affect broad containment of opinion and have added the paper with the lead author of Paraskevas to this paper as mentioned above.

Reviewer B:

Although this manuscript starts off well, it becomes a bit cumbersome.

COMMENT 1: Abstract and Main Text: No need to use the standard format: "Background-Methods-Results-Conclusions" in a review article. This format is only for original articles and systematic reviews. Furthermore, the text in each section is not appropriate to be included in this section. For instance, the "Results" section should report the results of a study. The authors simply review the results of different studies. That's not the same.

REPLY 1: Regarding the use of the format, we were advised by a member of the staff that we could use the standard format since our paper is both the introduction of a new method of discovery of unknown asymptomatic carotid stenosis and a rather thorough comparison with a number of other methods of either not giving the task sufficient attention or not accomplishing it so as to allow significant stroke reduction.

CHANGES IN THE TEXT: 1 We had a similar query from reviewer A. The authors did explain that the paper was both the introduction of a new method of rapidly screening seniors for ACS and, since there was either no recommendation for screening or at best incomplete methods and protocols, a review of the entire subject seemed in order. We have attempted to broadly modify the degree of opinion in the paper.

COMMENT 2: The whole "Discussion" section is largely un-referenced and reflects the authors' personal opinions. Again, this is not appropriate. It is also subjective and often irrelevant (e.g. the section with the 86 presentations at a meeting and the resistance in Medicine; what do these paragraphs have to do with the topic of this review article?

REPLY 2: We can understand the questioning of the reviewer of the author's concern with the complete focus at this time on the treatment of ACS, in which there is relatively little difference, whereas our concern is the near absence of focus on finding the silent ACS that causes most of the strokes due to carotid disease so that it can be treated. Only by finding the silent CAD in seniors and managing it before the stroke can we affect any large-scale reduction of strokes. It is the hope of the authors that publications such as this can result in greater discovery of the stroke potential disease so that it can be managed preemptively and strokes reduced, hopefully on an epidemiological scale.

CHANGES IN THE TEXT 2: As much as possible, the text has been pared down to explaining why the incidence of strokes has not decreased for decades and what in the authors opinion and in reality is the cause and is necessary to affect a breakthrough reduction in strokes.

COMMENT 3: There is no need whatsoever to underline whole sections of this manuscript. I have never seen any similar thing elsewhere.

REPLY 3: The authors agree and were only using the underlining to differentiate that text from the immediately preceding opinion of the USPSTF.

CHANGES IN THE TEXT 3: The opinion of the USPSTF was changed to a bold presentation to differentiate it from the authors following response from which the underlining was removed.

COMMENT 4: Author LG should avoid excessive self-citations. There is a self-citation to personal achievements 6 times in this manuscript. That is not particularly interesting for the average reader of this article.

REPLY 4:

It was noted that there were many references to one of authors. But this is a new technique developed by the author LG for which there were virtually no other references on the QCS. When other articles did have relevant and important implications, they were included.

CHANGES IN THE TEXT 4: None possible.