Reviewer’s report

Title: Risk factors and clinical presentation of craniocervical arterial dissection: A prospective study.

Version: 1 Date: 4 June 2012

Reviewer: Michael Haneline

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The authors portray this case-control study as a prospective research design, but in reality it is a case-control design wherein the subjects will be questioned soon after they become cases. The data that is collected will still be retrospective. This methodology, perhaps better termed contemporaneous than prospective, has certain strengths, but it also has weaknesses. For instance, patients interviewed soon after suffering a stroke may be physically and emotionally disturbed to the point that they cannot respond as coherently as someone who has had some time to heal.

The stated purpose of the manuscript is to “…investigate the presenting clinical features and pre-existing health status of CAD patients # 55 years in order to identify risk factors and describe the common early clinical features.” However, too much emphasis is placed on cervical manipulation as a risk factor which may introduce a bias that distorts genuine associations. This reviewer strongly recommends that the manuscript be revised to deemphasize this potential association and weight it the same as the other risk factors.

DISCRETIONARY REVISIONS

1) The first sentence, second paragraph on page 2 of the Background section would read better if “which have been undertaken” was deleted, “are” was changed to “were”, and “do” changed to “did”. The next sentence should also be changed as follows: “may include” to “may have included” and the second half of the sentence should be separated into a sentence on its own.

2) The first sentence, third paragraph on page 2 of the Background section is a run-on. Please divide it into 2 or 3 separate sentences.

3) Please delete the first use of “under 55 years” in the section under the heading “Cardiovascular factors” because it is provided below in the list.

MINOR ESSENTIAL REVISIONS

1) The first sentence, first paragraph in the Background section on page 1 states that CAD is increasingly being recognized as a major cause of ischemic stroke in younger adults. However, this condition is a well-known cause of ischemic stroke in younger adults and has been reported in numerous studies over the past several decades so its recognition is not really increasing any more. Thus, please delete “increasingly being recognized”.

2) The second sentence, second paragraph in the Background section on page 1 is somewhat unclear, because while sometimes CAD post-manipulation is due to inadequate differential diagnosis, the condition often does not manifest symptoms that would lead a prudent practitioner to make that diagnosis. Moreover, CAD is notoriously difficult to diagnose, especially in its early stages when patients are more likely to seek manipulative treatment. Perhaps it would be clearer if the second half of the sentence was replaced with something like this: “...whether some patients already have CAD in its early stages when it is difficult to diagnose.”

3) The first sentence, second paragraph in the Background section on page 2 mentions several previous “prospective” studies, but other important studies are missing (e.g., Norris et al and Smith et al immediately come to mind -- references listed below). Please consider these studies and search for others as well. Discuss and contrast their work with what you have planned.


4) Given that this topic has been investigated by a number of researchers using a similar methodology, the authors must provide a rationale and justification for conducting yet another CAD etiology study. Explain what is expected to be discovered that has not already been reported.

5) Cervical spine manipulation is referred to as a type of trauma at several places in the manuscript, but this is actually incorrect. While it has been hypothesized that cervical spine manipulation may be a trigger of CAD, so has backing up a car, watching an airshow, having ones hair shampooed at a beauty parlor, etc., none of which are traumatic events. To put manipulation alongside sports activities that commonly place gross injurious strains on the neck, as well as with direct and indirect trauma is imbalanced and may lead health care providers who provide this type of treatment to needlessly discontinue using it or may prevent other health care providers from referring patients for manipulation. Therefore, I recommend that you explain more about the difference between frank trauma and what has been referred to in the literature as “trivial” trauma and how manipulation fits into the latter category along with other common non-traumatic neck movements.

6) Please describe the timing of the structured interviews in the Methods section. Will the timing be the same for all participants? Patients may be emotionally charged and/or confused soon after admission which could distort their responses.

7) Please describe how selection bias will be controlled. For instance, who will determine which patients become cases? Will they have access to the patient’s history before deciding whether to accept the patient as a case (i.e., will they be blinded)?
8) Please indicate who will conduct the structured interviews and describe how they will be trained. Will they have any freedom to deviate from the interview script? If yes, how much freedom? This information is needed in order to assess the probability of interviewer bias.

9) The interview script should be written to the level of a person who only graduated from about the 7th grade. The term “palpitations” is used in item 3, which would likely be above that level. In item 6 of the interview script both “difficulty with your speech” and “difficult speaking” are included in the same sentence, which is redundant.

10) Item 7 in the interview asks whether the subject felt nauseous or vomited. Please add “as a result of the dizziness or loss of balance”. Otherwise, patients who respond that they vomited as a result of a migraine, for instance, could distort the resulting data by classifying them as being dizzy.

11) Item 1 in the Risk factors section of the interview should be reworded. Currently the phrase “have you had done” does not fit with some of the responses below it; “heavy lifting”, for instance. The section on manual treatment in this section places too much emphasis on these procedures as compared to the other risk factors. This emphasis may be result in it becoming a leading question. As a suggestion, consider using this wording: “Any manual treatment of your neck such as manipulation, forceful neck turning, or deep massage to the top of your neck”.

MAJOR COMPULSORY REVISIONS

1) The second sentence, first paragraph in the Background section on page 1 gives the annual incidence of CAD as 2.5-3:10,000, which is incorrect. It should be 2.5-3:100,000… a ten-fold difference.

2) The second sentence, second paragraph in the Background section on page 1 implies that other authors have indicated that the mechanism of CAD etiology involves both a pre-existing intrinsic susceptibility AND a precipitating event, which is incorrect. Sometimes no discernible event occurs in the progression of CAD. The condition can be and often is completely spontaneous. In fact, this manuscript’s reference 17 indicates that 61% of CADs reported over a 10 year period were spontaneous.

3) The heading “Mechanical trauma” in the Measurement of risk factors for CAD section on page 6 uses the term trauma inaccurately. Please delete the word trauma altogether or replace it with “actions” or “activities”. The authors may defend their position by citing other researchers who have used the term “trauma” to define this category, but please consider that these other researchers have employed an inaccurate definition as well. Many CAD triggers (i.e., reports of activities that preceded CAD, but were not necessarily causally related) are considered normal activities and therefore should not be categorized as trauma. The same type of inaccuracy in which neck manipulation is represented as “mechanical trauma” occurs in the first sentence, second paragraph on page 9 of the Discussion section. As a suggestion, consider writing something such as: “In the case of recent neck manipulation, the study will allow more detailed
information to be gained on the nature of the forces involved and direction of movement of the neck." The next sentence will have to be reworded as well.

4) Also under the heading "Mechanical trauma" it indicates that “...If any trauma is reported, specific descriptive details of the amount of force involved and direction of movement of the head and neck will be sought from the participant.” yet there is no provision for this kind of dialogue in the interview script. Please clarify. Also, one must exercise constraint in applying much credence to patients’ descriptions of the vectors that they experienced during cervical manipulation. Please refer to the following study which reported on the difficulties patients had recalling how they were manipulated by a chiropractor. Lewkovich G, Haneline M. Patient recall of the mechanics of cervical spine manipulation. J Manipulative Physiol Ther. 2005;28(9):708-12.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.