Author's response to reviews

Title: Standardized Ultrasound Evaluation of Carotid Stenosis for Clinical Trials: University of Washington Ultrasound Reading Center

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Re

Standardized Ultrasound Evaluation of Carotid Stenosis for Clinical Trials:
University of Washington Ultrasound Reading Center

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Cardiovascular ultrasound

Dear Rosa

Enclosed is the revised manuscript describing the methods and rationale used at the University of Washington Ultrasound Reading Center for the evaluation of ultrasound studies submitted for the CREST (Carotid Revascularization Endarterectomy vs. Stenting Trial) and other studies of carotid artery stenting.

This paper is not an official CREST publication, because it includes the methods used in all of our ultrasound reading contracts, but will form the basis of all reports of CREST ultrasound publications and therefore will be referenced by all of those publications.

RESPONSE TO REVIEWERS
Liz Andrea V. Baroncini “raised some questions that should be clarified in future studies. NO CHANGES REQUESTED
David Russell NO CHANGES REQUESTED
Rosa Sicari “This reviewer would only separate the clinical vs. the research use of vascular ultrasounds. Please also propose a practical algorithm for patient evaluation.”

The following revisions have been made to address these requests:

REVISIONS
ABSTRACT
A sentence has been added to the end of the abstract

Because the goals of research examinations are different from those of clinical examinations, screening and diagnostic clinical examinations may require fewer velocity measurements.
CONCLUSIONS

Paragraphs have been added to the end of the conclusions

Research examinations are exploratory, designed to answer a variety of questions. Usually, only a portion of the data gathered in a research protocol is found to be relevant to the questions finally addressed. In contrast, clinical examinations should be designed to efficiently determine whether each patient has a specific treatable condition and whether treatment is likely to improve their quality of life. To refine advice on clinical examination methods, the UWURC will compare pairs of Doppler velocity measurements acquired under the research protocol to address the following questions in future publications:

1) Are three velocity measurements in the CCA necessary to:
   a. identify CCA disease?
   b. provide a reference denominator for ICA/CCA ratio calculation?
2) Are measurements in the ECA and VA important to the clinical evaluation?
3) Do contralateral velocities decrease when an ipsilateral stenosis is treated suggesting that:
   a. intracranial cross-collaterals are present?
   b. ipsilateral intra-stenotic velocities might be reduced due to collateral flow?
4) Are particular velocity values or ratios predictive of complications during revascularization?

The first two questions relate to potentially simplifying the clinical examination by omitting superfluous measurements. The third question addresses a cofactor in the correlation between Doppler velocities and angiographic arterial diameter measurements. The fourth question suggests that additional inferences might be derived from a complete clinical examination including modulating the predicted risk of stroke.

Of course clinical carotid examination should be divided into two examinations: 1) screening examinations with a high sensitivity and acceptable specificity for internal carotid artery stenosis which can be carried ou in a non-specialist primary care setting, and 2) diagnostic examinations with high specificity for severe carotid stenosis with “vulnerable” plaque to assure that high risk patients are directed to appropriate treatment. When carotid examinations according to protocol have not been available, the UWURC has accepted data from “clinical examinations” to complete time points in the data set. The minimum data included in the studies have been single velocity measurements from the ICA and CCA on the evaluated side. Demonstration of a single end diastolic carotid velocity exceeding 1.4 m/s is universally accepted as proof of carotid stenotic disease, but verifying a non-stenotic carotid bifurcation requires more documentation.

We hope that these revisions are satisfactory to the reviewers
Sincerely

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