Author’s response to reviews

Title: Pulse Wave Velocity and Carotid Atherosclerosis in White and Latino Patients with Hypertension

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Version: 3 Date: 20 March 2011

Author’s response to reviews:

3/18/11

Dr. Robin Cassady-Cain, PhD:

In addition to the changes noted below from 1-28-11 I have added a sentence on written informed consent as directed.

Thank you for the opportunity to revise and resubmit our paper. I have responded to all editorial requests. The paper has been changed from Landscape to Portrait and a modified Table 3 in Landscape is enclosed. I have added all author contribution and competing interest information and responded to all the individual scientific reviewers below in italics. I enclose a revised manuscript in tracked changes for your review.

We appreciate your willingness to allow us to revise, and offer the following points and modifications that support the novelty and value of our study.

1. I think Dr. Tillin’s point (below) about the lack of value of hsCRP is a point of novelty that was under-emphasized yet very relevant given recent publication of the 2011 ACC/AHA Prevention guidelines which similarly suggest that this measure is a Class III recommendation of limited utility. We hope the addition of this strengthens the timeliness and the critical message of the paper since this test is over-used in the US and may offer little discriminatory value in a safety net population. This has been added to the key words, discussion, and conclusion sections for greater emphasis.
2. Along those lines, we have added data for high cIMT (>0.8 mm) as a dichotomous variable demonstrating that C-statistics assessing discrimination for PWV, Alx and Framingham risk score were 0.72, 0.63, and 0.51 respectively. This makes the point that in a safety net population Framingham risk score alone is not a good predictor of preclinical atherosclerosis thereby adding to the literature suggesting poor prediction of events in minority populations as well. This has been added in methods and results.

3. Sociodemographic depravity is an independent risk factor for CVD and to date no studies have evaluated arterial stiffness in a safety-net population. We believe the findings are therefore novel and add to the literature that highlights potentially safe, non-invasive, and cost-effective ways to enhances risk prediction.

Reviewer: Therese Tillin

This is a cross-sectional study of associations between various markers of cardiovascular disease and carotid intima-media thickness as a measure of atherosclerosis in a mixed Latino and White non-Latino US safety-net population. Given the known ethnic group differences in cardiovascular events and mortality and the uncertainties as to mechanisms underlying these ethnic differences, this is an important area of study. The authors have explained their rationale and objectives clearly and this is a well written paper.

We appreciate the positive comments.

- it is not clear how participants were selected (consecutively? how many declined etc?) -how was your sample size of 177 arrived at?

This data came from our data-warehouse as outlined. Each person was screened consecutively by the nurse for eligibility and was derived during a pre-specified enrollment period. We apologize for this oversight and minor modification has been made to the manuscript.

-although you state that you found no interactions between ethnicity and associations between PWV and CIMT etc, your cutpoint of p<0.05 for interactions seems rather stringent in a relatively small sample and it would be helpful to have some indication of whether there was any indication of interaction, even if not statistically significant at the 0.05 level- since your key interest appears to lie in ethnic group differences. I would welcome further exploration in general of ethnic differences in these associations, but appreciate that the study is underpowered for this.
We agree with the reviewer and have provided the p-value for interaction specifically in the text.

-it may be helpful to show standardised regression coefficients for your CV risk markers in order to enable a more straightforward comparison.

We agree and have redone Table 3 to reflect standardised regression coefficients for the continuous independent variables

- Although you show a strong independent association between ankle-brachial PWV and CIMT, I'd prefer to see some consideration of carotid-femoral PWV for future study given that ankle -brachial PWV combines both elastic and muscular arteries and most authors admit that carotid-femoral PWV is more strongly associated with markers of atherosclerosis (and it's not difficult to measure)

We agree this is the Gold Standard and concede that future studies might utilize this method to optimally assess vascular stiffness within the aorta. This has been added to the limitations section on page #9. Nonetheless, we believe that the strong correlation between carotid-femoral and brachial ankle PWV coupled with its highly significant relationship to CIMIT in the current study suggests this technique still has value clinically.

- Given the increasing body of evidence that CRP adds little to conventional risk assessment or management, you could perhaps afford to emphasise more strongly the absence of association between CRP and CIMT in this bi-ethnic population.

We agree and have added more information on this in the discussion section on pages 8 and 9 and noted the new prevention guidelines which recommend against using CRP; this does add to the novelty and relevance of the study.

Level of interest: An article of importance in its field

We thank the reviewer

Reviewer: Francesco Mattace Raso

With Interest I have read the manuscript 'Pulse Wave Velocity and Carotid Atherosclerosis in White and Latino Patients with Hypertension ' written by Mori J Krantz et al. The research question is clear but it sounds already known. Moreover, one of the authors' great worries is that Latino are not enough represented in published studies and I do not think that they will solve this
problem with a study on 177 subjects (1/3 Latino).

We appreciate this comment and acknowledge our study sample size in the paper as a limitation, yet believe this population is poorly studied and makes the contribution to the literature novel.

Minor comments: I think the bren dis Philips, not Phillips

Our equipment suggests Phillips is the vendor.

It is not clear which PWV has been measured (carotid-femoral, brachial-ankle?); considering the numbers I would say the B-A.

This is correct; we apologize for the oversight and have placed this information in methods section on page 5. It is also discussed extensively in the limitations on page 8.

Third, I am impressed by the characteristics of the population: mean BMI 33kg/M2, 49% with Diabetes. Are these numbers representative for all Latino?

We agree this is a unique finding from our population and in the US the largest growing minority is the Latino population, which is disproportionately affected by obesity and diabetes. This population is therefore of significant interest given the potential long-term risk for development of atherosclerosis.

Level of interest: An article of limited interest

We appreciate this perspective, yet contend that a safety net population is critical to study given known contribution of sociodemographic deprivation to overall CV risk and the need to find tools to better quantify risk prior to the development of overt disease.

Quality of written English: Acceptable

We thank the reviewer.

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

We thank the reviewer.

On behalf of our team we hope the paper with the aforementioned revisions is now suitable for publication in BMC cardiovascular disorders. Please don’t
hesitate to contact me and I appreciate your time and consideration.

Sincerely,

Mori J. Krantz MD