Reviewer’s report

Title: Exposure to Ambient Air Pollution and Calcification of the Mitral Annulus and Aortic Valve: The Multi-Ethnic Study of Atherosclerosis (MESA)

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Reviewer: Michal Krzyzanowski

Reviewer’s report:

The analysis presented in the paper tests a hypothesis about the relation of the degree of calcification of mitral annulus (MAC) and of aortic valve (AVC) with the level of exposure to particulate matter (PM2.5) and nitrogen dioxide in ambient air. The authors compare the results concerning MAC and AVC with associations of a progression of coronary artery calcification (CAC) with the exposure, analyzed and published previously. The data have been collected in a framework of well documented study MESA, applying well established methods and using thorough quality assurance protocols. Though the analysis suggests an association of the prevalent MAC and AVC, as well as of the changes in MAC with PM2.5, all associations are statistically nonsignificant. The authors suggest that this is the result of small sample size and low frequency of MAC and AVC, and propose to test their hypothesis in a larger sample. While this conclusion might be correct, its strength would increase and further studies would be facilitated if some additional data are shown or further analyses are performed in the available data set. Possible questions are:

- Is there any tendency for higher adjPRR and stronger relation of annual change in MAC and AVC with air pollution in older subjects? Results in Table 1 suggest that the calcification process is age-related and it might be that the influence of air pollution is restricted to older people.

- What is the impact of MAC and AVC assessment error on the results? This could be indicated by the proportion of people with MAC or AVC found in the first study but not in the follow up.

- Would the relation with the exposure be stronger if the analysis would be restricted to subjects (close to 50% of the study group) with CAC>0?

- Prevalence of smoking is lower in groups with AVC and MAC. These subjects are also older and more often under medication. What is the proportion of ex-smokers in these groups? Have this category been included in the "smoking status" variable?

- What was the rate of change in AVC and MAC in subjects with various AVC / MAC status at the baseline? This should be included in Table 1.

- Has the baseline status been included in the regression models for AVC / MAC change?
- Individually-weighted exposure data were defined in the Methods section but the results of the analysis using this indicator are not mentioned. Have they been similar to the main analysis?

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