Reviewer's report

Title: Cross sectional associations of epicardial fat with coronary calcification, insulin resistance, markers of inflammation and fibroblast growth factor-23 and in stage 3-5 chronic kidney disease patients

Version: 2 Date: 28 August 2012

Reviewer: AJAY YERRAMASU

Reviewer's report:

Minor Essential Revisions:

1. The aim of the study is to explore the association of EFV with CAC and conventional risk factors including Metabolic syndrome and Insulin Resistance. The authors have suggested that in the multivariate analysis, EFV is higher in patients with Metabolic syndrome and Insulin Resistance. However as shown in the study by Yerramasu et al (reference 11) and Rosito et al (Circulation. 2008 Feb 5;117(5):605-13), associations between EFV and Metabolic syndrome were not significant once adjusted for other measures of obesity. I would suggest repeating the multivariate analyses using Metabolic syndrome, Insulin resistance and CAC score as outcome variables and EFV along with other measures of obesity (waist circumference or BMI) and relevant conventional risk factors as the variants in the model. This will help us to show if EFV is independently associated with metabolic risk factors and coronary calcification.

I would also suggest including the findings from the above studies in discussion, especially the fact that EFV is not independently associated with metabolic syndrome after adjusting for other measures of obesity but it is associated with CAC score, suggesting a local paracrine effect.

Discretionary Revisions

1. On page 12, the authors state that "The CAC score detected by MSCT represents calcification arising from both the intimal blood vessel layer (where traditional CVD risk factors are known to impact) and the medial blood vessel layer (where kidney-related CVD risk factors including abnormal bone and mineral metabolism parameters are known to impact) [36]". I thought that calcification in coronary arteries is predominantly intimal and represents atherosclerosis unlike other vascular beds where medial calcification due to other factors is possible. Is this different in patients with CKD? Perhaps the authors can elaborate on this.

2. If the authors have the entire CAC volume dataset, why did they measure EFV from a single slice? I guess saving time could be one reason, but they have quoted only one study that showed single slice EFV is related to total EFV. Further evidence in this regard would be useful and could the authors consider measuring total EFV in a subset of patients and see how well it correlates with
single slice EFV in this study?

3. The authors could consider including a figure that shows the method of EFV measurement from single slice CT (a cross sectional image with the EFV highlighted), that would be of help to the readers not familiar with the cross-sectional CT anatomy.

4. Most of the other studies on this subject included Hounsfield units -30 to -190 to represent fat voxels, unlike the current study which included the range of -30 to -230 (is there any specific reason for this?)

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

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I have no competing interests to declare