Author's response to reviews

Title: Relationship between epicardial adipose tissue, coronary artery disease and adiponectin in a Mexican population

Authors:

Teresa G Yañez-Rivera (teresayanezr@yahoo.com.mx)
Manuel A Baños-Gonzalez (manuel_banos@hotmail.com)
Jorge L Ble-Castillo (iblecastillo@hotmail.com)
Manuel E Torres-Hernandez (thmanuel@hotmail.com)
Jorge E Torres-Lopez (jetorreslopez@hotmail.com)
Gabriela Borrayo-Sanchez (gabriela.borrayo@imss.gob.mx)

Version: 2 Date: 11 August 2014

Author's response to reviews: see over
Response to Reviewers

Referee comments 1:

Major Compulsory Revisions

- Results page 9 and Table 4: How were the parameters for multiple regression analysis selected? There is no mention of a univariate association of each of them with CAD and, for instance, on page 8 it is waist-hip ratio that was different in CAD+-, not waist circumference.
    Response. We appreciate the observation and a new paragraph was included in page 9 Variables, consisting of those with p values < 0.05 by univariate analysis were further assessed by multiple logistic regression analysis. We had an unforgivable mistake, in Table 3, waist circumference was changed by waist-hip ratio.

Minor Essential Revisions

Page 4, lines 4-7: "However" appears three times. Please cut to one.
    Response. We agree with this observation, we cut to one.

- Page 5, line 5: readers might not be familiar with those particular cut-offs. Ref. 16 should be put also immediately after "80 cm in women".
    Response. We changed the reference 16 according to the observation

- Page 6, Evaluation of...: since measurement of epicardial fat thickness is far from routine but also far from being universally standardized, references should be added in this paragraph showing similarities or differences in methods between this paper and others.
    Response. We thank for this observation, we introduced a sentence in page 6, lines 15-16: The reliability of transthoracic echocardiography for measuring EAT thickness, has been confirmed by its good correlation with magnetic resonance imaging.

- Page 7, last three lines: this is a result and should go in the Results sections before dealing with ultrasound measures.
    Response. We agree with the observation, the lines were changed in results section, on page 8, lines 4-6.

- Page 8, Results, Clinical ch., line 2: this sentence is missing something.
    Response. We agree, the sentence was modified to “our patient cohort consisted of 119 subjects with CAD (77.7%) and 34 subjects without CAD (22.2%)”.

- EAT thickness and...: "range 0-9.8" and "range 0-11.8" seems in contrast with Methods, page 6, where a measurement in thickness is stated to be considered if >1 mm. Please clarify the issue.
    Response. We appreciate your important observation. We had some patients with EAT thickness < 1 mm. We have removed the paragraph in method section to avoid contradictions. Moreover, ranges were eliminated because SD as a dispersion measurement around the mean was included.
"Data not shown" should be omitted. 
Response. “Data not shown” was eliminated

- Association of epicardial adipose tissue...: as epicardial tissue could be
determined by body size rather than adiposity, all significant and non significant
correlations should be shown: height, weight, body surface area, BMI, waist, hip,
waste-hip ratio, waist-height ratio, accurately choosing the variables for the
subsequent multivariate analysis.
Response. Table 3 was modified to include all the significant and the non significant
correlations.

- Discussion, page 10, last three lines: it seems unplausible that the paracrine
effect of EAT exerts itself directly determining an atherosclerotic stenosis in a
 discrete anatomical site in a coronary artery. An effect on the whole coronary
circulation, not to mention the endocrine effect on the systemic circulation, is
much more biologically plausible. Please remove the sentence about the lack of
association.
Response: We thank the reviewer for this important observation, we removed the sentence
about the lack of association.

- Discussion, page 12, lines 8-9: it is not clear that here we are not talking about
echocardiography in general, but with echocardiographic measurement of EAT.
Response. We have omitted a sentence and the ref 29 to improve understanding.

- Table 1 and caption: "Obesity was defined as increased waist circumference" is
unacceptable. If this is the definition, "obesity" can be replaced by "central
obesity".
Response. We agree with this important observation, Table 1 was modified to include
“central obesity” instead of “obesity”.

- Table 2: the mention of ejection fraction only can not be termed
"echocardiographic findings". Either describe at least basilar echocardiographic
characteristics of the hearts, or remove even ejection fraction and describe
adipose thickness only, possibly removing the whole table and putting them in
the text.
Response. We thank the reviewer for this observation, we have removed “ejection fraction”
data from the table and put it in the text. In the table 2 only the EAT thickness values is
showed.

- Table 3 should specify "univariate" correlations.
Response. “Univariate correlation” was included in the title of Table 3.

- Table 4 is not clear. Is "OR" the adjusted beta index? Or the variation with 1 SD
or one unit change in the selected parameters?.
Response. Effectively Odds Ratio (OR) correspond to the adjusted exponential of the B estimate obtained from the multivariate analysis.

Referee comments 2:

They have described a thickness by transthoracic echocardiography between 5.39 and 4.00 mm in the Mexican population. The difference between CAD and non CAD is quite low because they have also similar BMI.

Response. We agree that only a modest but significant difference was observed between EAT in CAD- and CAD+ groups. This low difference could be partially attributed to the similar BMI values between groups. It is known that epicardial tissue is correlated with fat deposits and specially with abdominal fat. In our study, most of the patients exhibited high values of waist circumference.

-Some authors suggested a EAT thickness > or =3.0 mm as an independent factor of CAD. In this way, all the population is in high CAD risk.

Response. We appreciated your observation, however, there is not a consensus about the EAT thickness cut-off, and the differences between populations have been well known. Although, all the study population could have a high CAD risk, our findings show that this risk is higher among patients exhibiting increased EAT thickness values.

-The thickness values were different than those described by another authors because the BMI of the study population is also different.

Response. We agree with your observation, however, not always an association between BMI and EAS thickness is observed. Jeong in a group from Korea observed a mean =6.30 in a Korean population with BMI equal to 24. Eroglu et al in Turkey reported 6.9 in CAD+ subjects with obesity and overweight. In general our values seem to be lower in CAD+ subjects in relation to other studied populations.

-The authors have not found a correlation between epicardial fat thickness and the number of stenotic vessels but it was described a differential epicardial fat thickness among patients with unstable (4.0 mm) or stable angina (3.0 mm) or atypical chest pain (1.5 mm).

Response. Indeed, some authors have informed a relationship between EAS thickness and the severity of CAD, however, we did not find such relationship. On the other hand, we did not perform an analysis on the clinical manifestation of the disease.

-It is very important to know the presence of Heart Failure because in chronic heart failure patients there is a reduction of EAT thickness.

Response. We thank for this observation, we also think that would have been interesting to have obtained this information. Our population was in general stable with >40% ejection fraction, nevertheless, a precise evaluation of the heart failure was not considered in our objectives.