Author's response to reviews

Title: Ultrasound Study of Carotid and Cardiac Remodeling and Cardiac-arterial Coupling in Normal Pregnant and Preeclampsia Women

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Author's response to reviews: see over
Dear Editors of BMC Pregnancy and Childbirth,

We are the authors of “Ultrasound Study of Carotid and Cardiac Remodeling and Cardiac-arterial Coupling in Normal Pregnant and Preeclampsia Women”.

We greatly appreciate you and the reviewers for your wonderful comments and suggestions. The following are our response point by point to the comments from the reviewers. Corresponding changes have been made in the text, which were marked in red. Please check. Thank you again for your great help on improving our manuscript. If there are any other things we need to do, please let us know. Thank you.

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Response to Reviewer Asma Khalil:

Question 1. The authors state that the measurements were performed in supine position. This position might be associated with significant vascular changes, e.g. supine hypotensive syndrome, in particular that most of the measurements were performed in the third trimester.

Answer 1. Thank you for your question. We totally agree with your concern. While the standard position for carotid ultrasound examination is the supine position. It might be interesting to observe the vascular hemodynamic changes with different positions in these pregnant women in the future.

Question 2. Reference normal values for non-pregnant age-matched women were 0.12 and 8.70 mm² for carotid relative wall thickness and cross sectional area respectively (data not shown). The authors should provide a reference or the data.

Answer 2. Thank you for your suggestion. The normal values we calculated for the non-pregnant age-matched women were 0.12±0.03 and 8.70±2.07 mm² for carotid relative wall
thickness and cross sectional area, respectively. This has been added in Methods on page 7, line 5-6 and in Results on page 8, line 2-3 from the bottom.

**Question 3.** Was a Power calculation performed for this study? The authors should describe it in the statistical analysis section of the Methods. How could they ascertain that their negative findings (e.g. the arterial ventricular coupling in patients with preeclampsia and the follow-up data morphological and functional parameters were comparable to controls).

**Answer 3.** A power calculation performed before the study, using $E_a/Ee$, indicated that 21 participants were required for each group. According to the preliminary experiment, $E_a/Ees$ were $(0.22 \pm 0.1 \text{mmHg} \cdot s^2/\text{ml} \cdot \text{m})$, for the Preeclampsia group and $(0.30 \pm 0.1 \text{ mmHg} \cdot s^2/\text{ml} \cdot \text{m})$, for the Normal group. The significance level was defined as alpha=0.05. After calculation, the power was approximately 0.81. The difference we originally planned to detect was $0.08 \text{ mmHg} \cdot s^2/\text{ml} \cdot \text{m}$. The above has been added in Statistical Analysis.

We would like to change “the arterial ventricular coupling in patients with preeclampsia and the follow-up data morphological and functional parameters were comparable to controls” to: “the arterial ventricular coupling in patients with preeclampsia showed no significant difference with those in controls.” Please see page 9, line 13-14.

**Question 4.** Did the authors test the data to see whether the values of the key parameters are normally distributed or not? If not, non-parametric tests should be used.

**Answer 4.** Yes, we tested and they were normally distributed. Thank you.

**Question 5.** The authors included Nulliparous women only. They should justify this.

**Answer 5.** In order to exclude the influences of parity on the cardiovascular parameters, we only included Nulliparous women in the current study.

**Question 6.** Some of the vascular parameters in this paper are significantly correlated to the blood pressure. Have the authors attempted to correct for this e.g. using regression analysis?

**Answer 6.** Yes, we did the regression analysis. The significance still existed after correcting for the blood pressures.

**Question 7.** The authors should comment on the strengths of their study.

**Answer 7.** Thank you. To our knowledge, this study was for the first time to explore both the cardiac and carotid remodeling and their coupling in preeclampsia women.
Question 8. The authors should mention more details on the follow-up data.

Answer 8. Thank you for your suggestion. We had added a table (Table 6) regarding the follow up information.

Question 9. The authors should elaborate on the clinical or scientific implications on their study findings.

Answer 9. Thank you for your suggestion. The findings of the our study indicate that both the cardiac morphology, function and the larger elastic arterial stiffness significantly change in preeclampsia women. These changes might also be associated with the increased cardiovascular diseases in these preeclampsia women in later life, suggesting that corresponding care might need to be taken for these special group of women during their pregnancy and postpartum. These information has been added in the text in red on Page 10 and 13. Please check. Thank you.

Question 10. The brachial blood pressure measurements were taken using an oscillometric device (Collin). Is this device validated in pregnancy?

Answer 10. This device has not been validated in pregnancy. But it has been used routinely for measuring blood pressures in a variety of patients, and it has been proved to be accurate.

Question 11. Table 3. The abbreviations should be stated in the legend.

Answer 11. These has been added. Thank you for your reminding.

Question 12. The English in this manuscript needs some attention.

Answer 12. Thank you for pointing this. We have carefully checked the English of this manuscript. If there are anything else that we need to correct, please let us know. Thank you very much for your precious suggestions.

Response to Reviewer 2

Question 1. As it is also explained in the text, the number of patients enrolled in the study is an important limitation. It is not mentioned if these women had a severe or not preeclampsia, although in Table 1, the gestational weeks at delivery was 40 in the preeclampsia group.

Answer 1. We are very sorry for not including these information in the paper. These women were severe preeclampsia women. We apologize that the delivery weeks was input in the
wrong line. It should be 37±1 for the preeclampsia group and 40±1 for the normal group. It has been changed in the text. Please see table 1. Thank you.

Question 2. Table 1. Women with preeclampsia had more weeks at delivery than normal women?
Answer 2. No, it was a mistake. We apologize for it. It has been corrected. Thank you for noticing this.

Question 3. The number of follow up patients is also very small. Why the rest of patients did not have this follow up after delivery? This should also be mentioned in the text.
Answer 3. We also feel bad about this. They could be not followed up for a variety of reasons. Some of them could not be reached any longer via the contact information they left for us, some of them lived a little bit far from our hospital and they feel it is difficult to come back for a follow up study.

Question 4. In my opinion, in the text it is not quite clear how the patients were enrolled for the study.
Answer 4. All women were recruited from our routine antenatal clinic between January 2010 and July 2012. All were nulliparas, had singleton pregnancies and had no other risk factors for arterial stiffness including smoking, sleep apnea, in vitro fertilization conception, diabetes and hypercholesterolemia. The diagnosis of preeclampsia was based on the guidelines of the International Society for the Study of Hypertension in Pregnancy (ISSHP) Women with gestational hypertension and chronic hypertension were excluded. More detailed information were added in red in Study populations on page 5.
Please let us know if these information is not adequate and what else information you suggest we should put in. Thank you very much.