

Dear editor of *World J Clin Cases*

Thank you for your e mail

We would like to present our thanks for considering our work for publication

We like to thank the reviewers for their effort to improve the quality of the submitted work

We hope the changes that we made will meet your approval

Reviewer #1:

1. I would suggest reporting intra- and inter-observer variability for AUC-ICA measurements.

Response thank you for raising that issue. It was addressed in the line 214-216, page 9 And line 424 page 16.

2. Please introduce metformin treatment (dosage and duration) in the methods.

Response done; kindly see line 157-159 page 7

3. Please check abstract and text for typos (i.e. [abstract] metformin tab – 500 gram should be 500 mg; similarly, in results section there is 500 gm instead of 500 mg)

Response We regret that typo in reporting ; correction was made thank you for the highlight.

Reviewer #2:

1. From our experience, the measurement error of intima-media thickness is large

Response

Dear reviewer we totally agree ; the error in measurement of the intima media thickness is sometimes so large from our experience too, for that we have decided to use the concept of AUC to overcome this problem; it was our rationale and drive for using the concept of AUC ; thank you for raising this critical point.

However, AUC can not be measured directly from the Doppler devices, at least the ones available in Iraq, which is why we used a simple software that is freely downloadable from the web to measure AUC from repeated measurements of the heights of systolic and diastolic blood waves to overcome this problem. Remember that numerical methods are a very efficient tool to measure mathematical models. The software uses Simpson's 1/3th rule to measure AUC.

So far, our measurements have shown a significant correlation between AUC and HOMA_IR.

2. **do authors use relevant auxiliary software or special features of the instrument? It is suggested to add image descriptions.**

Response

Dear reviewer, we have added a new photo with better resolution; we have re-written the method in more clear way; and added image descriptions

Kindly see line 214-216 Page 10

Line 225-229 Page 10

A sample of ICA Doppler is shown in Figure 2. In this picture, we measured the different heights of the Doppler wave (demarcated by dots in Figure 2 A)as it went up and down with a facility supplied by the ultrasound device. Depending on the width of the wave, these measurements averaged between 8 and 10; see the horizontal orange line in Figure 2 A). The measurement of the heights represents the speed of blood in the systolic and diastolic velocities. The calculated heights were put in an Excel table to analyze later with simple, free software called GRAPH, which can be downloaded from:

<https://www.padowan.dk/download/> [19].

In Figure 2 B a graphical simulation of the internal Carotid Artery Doppler wave in Graph soft ware is shown ; with the different heights (demarcated in red dots) used to measure the systolic and diastolic blood flow for the calculation of AUC.

3. **The ultrasound images are suggested to select the photos saved by the instrument or electronic images reserved by the reporting system, which looks neater and more beautiful than the scanned printed images. The baseline in Figure 3-c seems skewed.**

Response

Thank you for your carfull comments; we have updated the photo with improved resolution; we hope they will meet your approval.

Reviewer #3:

1. **In full text, fasting blood glucose is not medical terminology; please use glucose instead of sugar.**

The response has been made as suggested. Thank you for raising this point

2. **Please specify whether there is normal distribution in all your continuous data. If there is no normal distribution, please express median plus interquartile range instead of mean \pm standard deviation, and please use the Kruskal-Wails test instead of the One-way ANOVA test when assessing the statistical data differences at 3 time points. 3**

Response

data were normally distributed and checked by the Shapiro Wilk test, and ANOVA was used; we added the comment in the text; kindly **see page 10 line 261.**

Our statistician; greatly appreciated that comments, sir, and sent his response :

The test used for checking data normality was the Shapiro-Wilk test. In case of any inconsistency, whether in distribution or homogeneity, it gives an immediate warning, no such warning was received in any analysis of the variables listed in table one. In addition, it uses Friedman ANOVA universally for one-way ANOVA. It should be mentioned that we skipped pairwise comparisons from the table as they were all significant except for one variable. We acknowledge greatly the receipt of your kind comments about the choice of ANOVA type used to compare the 3 major groups in the study. Medcalc ; The software we used to calculate various variables in table one uses Friedman ANOVA universally for one-way ANOVA after checking both the normality and homogeneity of the data.

3. **Table 1 and 2, please use the unified format for all parameters and please use the same number of digit for all P values.**

Response done; all suggested changes were done