

The authors submitted a revised version of the original paper, with point by point responses to the questions asked initially.

While there were some changes that improved the manuscript quality, there are still some points that need to be addressed before a publication recommendation.

2- Across the article, the terms Sudoscan and ESC are used interchangeable. This should be avoided. The technique used is the Electrochemical Skin Conductance. The device used for this is called Sudoscan. The name of the device should not be used as a technique. Please clarify this throughout the text

Response: Thanks for your comment. We have checked the whole article and made changes.(line 199, 219, 221, 227)

While the changes made were adequate, they were clearly insufficient. Some examples of the incorrect use of the term Sudoscan as a technique and not a device:

Line 24 “SUDOSCAN was tested and evaluated with electrochemical skin conductance”

Line 58 “Sudoscan is a method”

Line 200 “The results suggested that sudoscan can be used as a clinical screening tool for diabetic neuropathy”

3- Clarification regarding SUDOSCAN-MDRD is needed. The authors do not explain this score or reference any publication in the Methods section. Why was this score used in the ROC analysis instead of the ESC values?

I have some reservations in using algorithms that are unknown to the authors, since they are proprietary of the firm that sells this specific device and, for that matter, impossible to scrutinize. However, the authors clearly state in the text this particular point (line 89) so readers can be aware of the fact.

6- Another point in the binary logistic regression is the choice of using the mean of the ESC from the 4 limbs. Since the authors chose to use the cut-off of 60 μ S to define normal vs abnormal, this dichotomic variable should be used in the logistic regression.

Response: This is a good comment. The main reason we used the average value of ESC instead of the binary classification value is that the registration data will reduce the statistical efficiency compared with the measurement data.

For example, one patient ESC11 and another patient ESC 59. Both are ESC abnormal, their binary classification value are the same, but there are great differences in clinical severity. Therefore, we choose original measurement data.

I have to disagree with the choice to use the original measurement data. The objective of this paper is to assess the potential role of ESC as a biomarker of microvascular diabetic complications. For that matter, the work should focus on cut-off values and their respective diagnostic value.

9- In the beginning of the Discussion section, the authors state that “patients with a lower ESC (<60 μ S) had 2.1-fold increased likelihood of having DPN, 2.4-fold increased likelihood of having DKD, 1.2-fold increased likelihood of having DR, than those with a higher ESC.” However, there is no reference in the results to this analysis. It is not clear where do these results come from.

Response: This statement is based on table 1. There were significant differences in presence of DPN (88.99% vs 42.86%, $P < 0.001$), presence of DKD (39.76% vs 16.40%, $P < 0.001$) and presence of DR (30.58% vs 25.53%, $P = 0.012$) between both groups. We have realized that this statement was not rigorous. So we changed this sentence to " patients in ESC normal (<60 μ S) group had 2.1-fold increased likelihood of having DPN, 2.4-fold increased likelihood of having DKD, 1.2-fold increased likelihood of having DR, than those in ESC abnormal ($\geq 60\mu$ S) group. " in the text. (line 179-182)

This analysis is methodological incorrect. The fact that in this particular group of patients there was 2.1 more subjects with DPN in the abnormal ESC group, does not mean that subjects with abnormal ESC have 2.1-fold increase in likelihood of having DPN. The same is valid for the other statements.

In order to assess this kind of relationship, the authors should use the binomial logistical regression, with a dichotomic variable of normal/abnormal ESC. The analysis of the odds ratios is what would allow for the authors to make this kind of statements.

7- The ROC analysis showed interesting results for the diagnostic value of the ESC, in particular regarding DPN, as expected. However, I do not understand the choice of comparing the AUC of ESC with other variables. Since the variables chosen for comparison were the ones used as gold standard for the definition of each condition, ESC would always shown poorer results. Also, it is not clear which cut-off value was used. 60 μ S? Other?

Response: In this study, we compared AUC of ESC with other variables because we want to explore the diagnostic value of ESC. In particular, we wanted to understand the gap between ESC and other gold indicators, and whether it can play an auxiliary or alternative role in clinical diagnosis. Cut-off value was showed in table 4.

The Results sub-section “ROC curve analysis : effective diagnostic value of ESC in diagnosing DPN” (Line 161) repeats data that is given in table 4.

I would advise to cut the text, since the results are well described in table 4 and figure 1.