

The authors submitted a paper in which they evaluated the performance of the Electrochemical Skin Conductance, measured with a Sudoscan device, as a potential marker of different microvascular complications in type 2 diabetes patients, namely diabetic neuropathy (DPN), diabetic kidney disease (DKD) and diabetic retinopathy (DR).

Additionally, the authors analyzed a derived score given by the device (SUDOSCAN modification of diabetic renal disease) also as a potential marker of DKD.

Each condition was determined according to standard international accepted criteria.

Subjects were divided into 2 groups according to ESC results (normal > 60 μ S; abnormal < 60 μ S).

The authors reported significant correlations between hands and feet ESC and several clinical variables.

The authors then performed a binary logistic regression analysis and found that a mean of the ESC from the 4 limbs was a significant independent predictor for DPN and DR. The authors also reported that the score SUDOSCAN-MDRD was also a significant independent predictor for DKD.

Finally, the authors performed a ROC curve analysis of the diagnostic value of hands and feet ESC for DPN and DR as well as SUDOSCAN-MDRD for DKD.

The authors then concluded that ESC, as measured by the Sudoscan device, has an effective, but limited, value as a diagnostic tool for diabetic microvascular complications.

Despite not being the first study to investigate this relationship, the article is interesting and has some strong points in its favor, in particular, the large number of patients studied, with a wide range of ages.

However, there are some points that need clarification before a publication endorsement.

Concerns:

- 1- The article would benefit from a thorough revision regarding the language used.
- 2- Across the article, the terms Sudoscan and ESC are used interchangeably. 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.
- 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?
- 4- In the results section, the authors stated that FESC was lower in males when compared to females (59.53 ± 21.66 vs 64.28 ± 18.89 , $P = 0.002$). However, when verifying these values with the raw data supplied, the p value obtained is not consistent with the one reported.

		Independent Samples Test								
		Levene's Test for Equality of Variances		t-test for Equality of Means					95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
FESC	Equal variances assumed	9.570	.002	-2.637	513	.009	-4.74967	1.80102	-8.28796	-1.21139
	Equal variances not assumed			-2.661	512.945	.008	-4.74967	1.78513	-8.25673	-1.24262

As can be seen in the picture above, the p value of 0.002 refers to the Levene Test For the Equality of Variances. The correct p value to be reported should be $p = 0.008$, since the Levene test suggests that the homogeneity of variances assumption is violated.

This is not an overly important mistake but should warn the authors to double check their results interpretation.

- 5- Regarding the binary logistic regression analysis, the results are somewhat confusing. What are the results of each model? Where all variables considered for the final models? Looking at Table 3, it appears that all variables were considered for the 3 models analyzed. If so, what is the clinical rationale to consider BMI, hypertension or eGFR for the DPN model? Or the clinical rationale to consider VPT for the DKD or DR models? This needs to be clarified.
- 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.
- 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 where the ones used as goal 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?
- 8- Additionally to the ROC analysis, the authors should clearly present sensitivity, specificity, PPV and NPV for ESC in each condition, in the results section, and not throughout the discussion.
- 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.
- 10- The discussion should be shortened around the main findings of the present article. Results of the study should be clearly stated in the Results section and not scattered though the discussion.
- 11- The authors state that “it is the first study to report the relationship between sudoscan and DR in T2DM”. However, Camion et al. 2019 (<https://doi.org/10.2337/dc18-2202>), reported lower feet ESC in patients with severe diabetic retinopathy.
- 12- The authors suggest that one possible explanation for the lower FESC in male, when compared to females could be “the fact that men are more likely to have

bad habits such as smoking". However, when looking at table 2, one notes that HESC had a higher and stronger correlation with smoking than FESC (-0.134 $p = 0.002$ vs -0.095 $p = 0.031$). With the current data, the authors cannot back up this statement.