Reviewer’s report

Title: Pulse wave velocity and cardiac autonomic function in type 2 diabetes mellitus

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Reviewer: Elif I. Ekinci

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Carotid femoral pulse wave velocity is independently associated with cardiovascular disease.

Pulse wave velocity is the gold standard method for assessing arterial stiffness.

Arterial stiffness is increased in people with diabetes

PWV independently predicts mortality

Chronic hyperglycaemia, hyperinsulinaemia, low grade inflammation and increased oxidative stress and AGES may contribute to increased arterial stiffness in people with diabetes.

The hypothesis for the current study is that following adjustment for usual atherosclerosis risk factor, that CAD is independently associated with abnormal PWV in people with T2DM.

290 participants with type 2 diabetes were recruited

Patients with AF, pacemaker were excluded, as were those with an eGFr < 30 and severe liver disease

PWV was calculated from measurements of pulse transit time and the distance traveled between the common carotid artery and the common femoral artery. The distance measurements were taken with a measuring tape by subtracting the distance from the suprasternal notch to the carotid from the suprasternal notch to the femoral artery at the sensor location

Patients with abnormal PWV were older, had higher arterial blood pressure and higher heart rate than those with normal PWV.

The investigators demonstrated that CAD assessed by determination of HRV was a significant determinant of abnormal PWV

However, it is possible that both arterial stiffness and CAD simply share similar underlying aetilogies including chronic hyperglycemia and hyperinsulinemia, formation of AGES and protein kinase C activation, low grade inflammation and endothelial dysfunction, as the authors have suggested.
Can the authors expand on the clinical implications of the study. Why would CAD lead to increased PWV? In particular can they expand more on the following statement please:

"These data reveal an additional common pathophysiological pathway that may explain the relationship between arterial stiffness and autonomic neuropathy" and can they expand on the following:

"Moreover, autonomic nervous system has been found to have a trophic influence on the structure of vessels and thus CAD may lead to arterial stiffening"

Is there any information regarding the underlying biological pathway for this ie how CAD has a trophic influence on structure of vessels?

It is interesting that there were no significant associations between PWV and conventional risk factors like age, smoking, microalbuminuria and lipid profile. Why might this be?

The introduction is too long and it could be cut down by half.

One limitation is that there are no non diabetic controls

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

No

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

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