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Cardiac autonomic neuropathy independently increases the risk for heart failure in patients with type 2 diabetes

Aim: The assessment of the association between cardiovascular autonomic neuropathy (CAN) and incident heart failure (HF) in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) study population.
Methods: This was a secondary analysis of ACCORD data including 7160 participants with no HF at baseline (mean age 62.3 years, 40.4% women). CAN was assessed by time-domain measures of heart rate variability (HRV) and QT interval index (QTI) based on short ECG recordings (10 seconds). The assessed HRV measures were the standard deviation of all normal-to-normal intervals (SDNN) and root mean square of successive differences between normal-to-normal intervals (rMSSD). CAN was defined as composite measure of HRV, QTI and heart rate. Multivariable regression models were performed to obtain adjusted hazard ratios (aHR) for incident HF in relation with CAN measures. Covariates included age, sex, race, treatment arm, current cigarette smoking, duration of diabetes, use of antihypertensive, glucose-lowering and antiarrhythmic medication, history of retinopathy, prevalent ASCVD, left ventricular hypertrophy, HbA1c, cholesterol levels and estimated GFR. Incident coronary artery disease (CAD) was recorded and used as a time-varying covariate.
Results: During the median follow-up of 4.9 years, 222 patients developed HF. After adjustment for confounders, lower HRV assessed by SDNN was associated with a higher risk of HF (aHR for the lowest vs highest quartile of SDNN: 1.70, 95% confidence interval [CI] 1.14-2.54) and participants with CAN (defined as lowest quartile of SDNN and highest quartiles of QTI and heart rate) had a 2.7-fold greater risk of HF (aHR 2.65, 95% CI 1.57-4.48).
Conclusion: CAN was independently associated with higher risk for incident HF in patients with type 2 diabetes.

Comments. This well-designed study proves the association of CAN with incident HF in a large population-based cohort of patients with type 2 diabetes. Furthermore, CAN was independently associated with a higher risk of HF after adjustment for a variety of known cardiovascular risk factors. The fact that the CAN-related risk for HF was independent of CAD suggests that silent ischaemia (angina/infarction) alone cannot explain the association but other mechanisms (AGE, electrical instability, microvascular damage, etc.) might contribute to the development of HF in patients with CAN. HRV and QTI were used for the assessment of CAN, which are sensitive measures of CAN and have prognostic value in predicting cardiovascular morbidity and mortality. This secondary analysis has some clinical implications for daily care as well: cardiovascular risk stratification should involve assessment of cardiovascular autonomic function in patients with diabetes and strategies improving cardiac autonomic function may help the prevention of HF.
One limitation of the study is the relatively short time of follow-up. Besides, applied measures and definition of CAN are considered sensitive but not the gold standard for CAN assessment that could affect data. Moreover, only symptomatic (clinically manifest) HF could be assessed, while no information on subclinical cardiac dysfunction was available due to the lack of echocardiographic studies. Subclinical cardiac dysfunction could affect a huge proportion of patients with type 2 diabetes. Systolic and diastolic HF were not distinguished as well.

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Reference. Kaze AD, Yuyun MF, Erqou S, Fonarow GC, Echouffo-Tcheugui JB. Cardiac autonomic neuropathy and risk of incident heart failure among adults with type 2 diabetes. Eur J Heart Fail. 2022 Jan 22. doi: 10.1002/ejhf.2432. Epub ahead of print.
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