

Which factors predict mortality in people with diabetic cardiovascular autonomic neuropathy

Aims: The study aimed at evaluating whether clinical attributes, autonomic testing findings and genetic variants, present at the time of diagnosis of cardiovascular autonomic neuropathy (CAN), are associated with increased mortality.

Methods: 124 participants with diabetes who had received a CAN diagnosis between 2015 and 2022 were included, among whom 25 were deceased. CAN diagnosis was based on cardiovascular reflex tests (CARTs), baroreflex vagal sensitivity and pressure recovery time during Valsalva maneuver. Electronic medical records were retrospectively reviewed for demographics, diabetes type, age at onset, duration, metabolic profile, diabetic polyneuropathy, retinopathy, hypertension, medications, cardiac disease, stroke or obstructive sleep apnea; and, if deceased, cardiac etiology of death. In a subset of 69 patients, previously identified genetic risk factors for idiopathic neuropathy and CAN were evaluated. Kaplan-Meier and univariate/multivariate Cox regression analyses were used to identify risk factors for mortality.

Results: Follow-up from time of CAN diagnosis was 150.5 ± 87.1 weeks. At diagnosis, non survivors were older and had a lower BMI (26.5 ± 5.3 Vs 30.6 ± 6.7 kg/m², $p=0.002$), more cardiac disease, abnormalities on a head-up-tilt test, neurogenic orthostatic hypotension (nOH) ($p < 0.0001$), and an abnormal QSART. In the subgroup with genotyping, a risk genotype for idiopathic neuropathy, rs147738081-CT, was more common in non survivors ($p=0.009$). In the covariate-adjusted Cox proportional-hazard survival model, older CAN-diagnosis age [adjusted HR 1.04 (1.01–1.07), $p=0.011$], decreased BMI [0.88 (0.81–0.96), $p=0.005$], and nOH [5.91 (2.01–17.35), $p=0.001$] remained significant risk factors for mortality.

Conclusions: Clinical variables expected to influence mortality risk were not significant predictors of mortality in this CAN cohort, as well as the severity of abnormality in cardiovascular tests, while age at CAN diagnosis, lower BMI and the presence of nOH were predictors of mortality. The results might inform both the development of guidelines for prevention and the design of larger studies to evaluate CAN mortality risk factors.

Comments. This Letter to the Editor, with a rich supplementary documentation, describes a retrospective evaluation of a small cohort with advanced diabetes and CAN, diagnosed with standard CARTs and additional autonomic tests, with the aim to disentangle the factors associated with mortality at 3 years of follow-up. The study has the limitation of small size, retrospective design, and the absence of a control group without CAN, but provides the interesting finding that independent predictors of mortality were not the expected risk factors as cardiovascular disease history, but lower BMI and the presence of neurogenic OH (and not the isolated supine hypertension). This confirms the worse prognostic value of OH compared to abnormalities in cardiac vagal tests, leaving open the questions whether lower BMI and OH play as surrogate markers of diabetes severity and whether specific autonomic tests and genetic variants might serve in a strategy to improve the prognosis.

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Reference. Chase BA, Pocica S, Frigerio R, Markopoulou K, Maraganore DM, Aunaetitrakul N, Epshteyn A, Barboi AC. Mortality risk factors in newly diagnosed diabetic cardiac autonomic neuropathy. Clin Auton Res. 2023 Sep 11. doi: 10.1007/s10286-023-00975-5. Epub ahead of print. PMID: 37695385.

<https://link.springer.com/article/10.1007/s10286-023-00975-5>