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No autonomic neuropathy without peripheral neuropathy?

***Aims*:** The aims of this study are (1) to estimate the prevalence or co-existence of cardiac autonomic neuropathy (CAN) in patients with diabetic peripheral neuropathy (DPN) with small and large fiber involvement; (2) to investigate whether the presence of painful DPN (PDPN) influences the prevalence of CAN, and (3) to establish a multivariate logistic regression model for predicting the risk of CAN based on thermal peripheral measurements in patients with type 1 diabetes (T1DM).
***Methods*:** Eighty participants [20 T1DM + PDPN, 20 T1DM + DPN, 20 T1DM-DPN (without DPN), and 20 healthy controls (HC)] were enrolled. The groups were matched on age and sex. DPN was determined by vibration perception threshold >25 V and ´probably neuropathy´ according to the Toronto consensus criteria. CAN was determined by cardiac autonomic reflex tests (CARTs) (≥ 2 abnormal CARTs). Large fiber involvement was determined by abnormal nerve conduction velocity or amplitude of the sural nerve. Small fiber involvement was determined by abnormal cold- or heat perception threshold (CDT, HDT) assessed by quantitative sensory testing (QST). After the initial analysis, the participants with diabetes were re-grouped based on the presence or absence of small (SFN) and large fibre neuropathy (LFN), respectively. The model of risk stratification was made by utilizing simple logistic regression followed by stepwise multiple logistic regression with backward elimination.
***Results*:** CAN was most prevalent in T1DM+PDPN (50%), followed by T1DM + DPN (25%) and T1DM-DPN and HC (0%). There was a significant difference between T1DM+PDPN and T1DM-DPN and HC. When re-grouping, 58% had CAN in the SFN group and 55% in the LFN group, while no participants without either SFN or LFN had CAN. In the regression model CDT and HDT (but not the cold or heat pain thresholds) were significant predictors of CAN. In the multivariable logistic regression model only CDT persisted and had a sensitivity of 64%, a specificity of 67%, a positive predictive value of 30% and a negative predictive value of 90%, with an associated AUC of 0.81 at the optimal cut-off of 27.0°C.
***Conclusions*:** These results suggest that CAN predominantly co-exists with peripheral sensory neuropathy and that the presence of some subtypes of PDPN might increase the risk. Peripheral thermal sensation is a poor predictor for CAN, although a CDT above 27°C makes its presence unlikely.

Comments. DPN and CAN are different manifestations of diabetic nerve damage, that are often described individually. Several studies have suggested concomitant development, while others have failed to show such co-existence. These results suggest that CAN primarily needs to be considered when DPN is present, independently from large- or small fiber involvement. The study also showed that CDT is a decent parameter to determine whether patients with T1DM have a risk of CAN. Moreover, CAN might be overrepresented in patients with PDPN. Strengths of this study are the well characterized and matched groups. Limitations are the small sample size and the fact that only one diagnostic method was used for CAN. A larger study with multiple assessments of DPN and CAN would be useful to confirm these results.

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Reference. Røikjer J, Croosu SS, Hansen TM, Frøkjær JB, Brock C, Mørch CD, Ejskjaer N. The co-existence of sensory and autonomic neuropathy in type 1 diabetes with and without pain. Acta Diabetol. 2023 Mar 7. doi: 10.1007/s00592-023-02062-7. Epub ahead of print. PMID: 36881186.

https://link.springer.com/article/10.1007/s00592-023-02062-7