

**Lack of consensus of best diagnostic tests for neuropathy in adolescents: could point-of-care devices be the answer?**

**Aim:** To evaluate the prevalence of neuropathy in adolescents with type 1 diabetes (DM1) applying confirmatory tests from the adult population for large fiber (LFN), small fiber (SFN) and autonomic neuropathy. Secondly, to evaluate the diagnostic accuracy of available bedside methods for neuropathy in adolescents.

**Methods:** Sixty individuals with DM1 and 23 healthy subjects participated in the study. All were aged 15-18 years and individuals with DM1 had a diabetes duration of  $\geq 5$  years. Confirmatory tests of diabetic sensorimotor polyneuropathy (DSPN) included nerve conduction studies (NCS), skin biopsies of intraepidermal nerve fiber density (IENFD), and autonomic nerve testing including quantitative sudomotor axon reflex test (QSART), cardiovascular reflex tests (CARTs), and tilt table test. Bedside tests included biothesiometry, DPNCheck<sup>®</sup>, Sudoscan, and the Vagus<sup>®</sup> device, and the diagnostic accuracy of bedside tests were compared to confirmatory tests using ROC analyses. The presence of neuropathy was defined applying the Toronto criteria classifying confirmed DSPN by NCS and IENFD for LFN and SFN, respectively. Findings from each test were defined as abnormal when below the 5th or above the 95th percentile compared to data obtained from the enrolled healthy control subjects.

**Results:** Adolescents with and without DM1 were similar on age (median, 17 years). Individuals with DM1 had a median (min-max) diabetes duration of 8.5 (4.6-17.4) years and a median HbA1c of 60.0 (41-93) mmol/mol. Reported prevalence of neuropathy in the individuals with DM1 was; 14% confirmed LFN, 2% confirmed SFN, 20% abnormal QSART, 8% abnormal CARTs, and 14% orthostatic hypotension. Additionally, 25-26% proved to have either subclinical SFN or LFN. The assessment of bedside tests demonstrated that sural conduction velocity screened by the DPNCheck<sup>®</sup> (ROC 0.73) and the HR response to expiration and inspiration evaluated with Vagus<sup>®</sup> (ROC 0.72) had acceptable diagnostic accuracy compared to the confirmatory tests.

**Conclusions:** Confirmatory diagnostic tests detect early neuropathic changes including LFN, SFN and autonomic neuropathy in adolescents with type 1 diabetes. Point-of-care devices including the hand-held electrodiagnostic device (DPNCheck<sup>®</sup>) and the Vagus<sup>®</sup> device proved to have acceptable diagnostic accuracy of DSPN.

**Comments.** The present study includes a full-scale approach for assessment of DSPN in adolescents from best available evidence providing important insight on the prevalence of DSPN in this relatively under-examined population. The study confirms early neuropathic changes as a relatively frequent finding in adolescents with DM1, stressing the importance of early prevention and management of modifiable risk factors to reduce the load of DSPN later in life. In the extensive workup of this study Rasmussen et al highlight a central challenge; the lack of consensus regarding protocols and cut-off values for assessment of DSPN. The impact of this challenge is stressed by the variation in reported DSPN prevalence in adolescents depending on the criteria and modality for assessment of LFN (14-57%) and SFN (2-62%). Point-of-care devices may provide valid measures of DSPN that are implementable in a broader setting than confirmatory tests that require expertise and are rarely feasible or preferable in the clinical setting. Rasmussen et al evaluate a broad range of bedside tests allowing us to weigh the accuracy of available point-of-care devices against each other. Available bedside methods could be valuable in future standardization of diagnostic evaluation of DSPN and deserve future evaluation of their efficacy across different populations and facilities.

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**Reference.** Rasmussen VF, Thrysøe M, Nyengaard JR, Tankisi H, Karlsson P, Hansen J, Krogh K, Brock C, Kamperis K, Madsen M, Singer W, Vestergaard ET, Kristensen K, Terkelsen AJ. Neuropathy in adolescents with type 1 diabetes: Confirmatory diagnostic tests, bedside tests, and risk factors. *Diabetes Res Clin Pract.* 2023 Jul;201:110736. doi: 10.1016/j.diabres.2023.110736. Epub 2023 Jun 3. PMID: 37276985.

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