Josine C. van der Heyden,[1,2,3] Erwin Birnie,[4] Dick Mul,[1] Henk J. Veeze,[1] Joleen H. Blok,[5] and Henk-Jan Aanstoot[1]

COMMENT ON MALIK

Which Test for Diagnosing Early Human Diabetic Neuropathy? Diabetes 2014;63:2206–2208

Diabetes 2015;64:e1 | DOI: 10.2337/db14-1472

Recently, Professor Malik (1) discussed the lack of an appropriate test for the early detection of diabetic neuropathy (DN). He questioned the utility of conventional neurophysiological and symptom-based tests before outlining potential small-fiber–focused techniques as measures of subclinical DN (SDN), as illustrated by the elegant techniques of corneal confocal microscopy (1). As improved glycemic control during the early stages of DN may prevent or delay nerve function deterioration, timely detection of SDN is important. The rapidly increasing prevalence of type 1 diabetes (T1D) in youth, resulting in longer disease duration and increased likelihood of developing SDN, underscores this unmet need for identifying early markers of SDN.

We agree with Professor Malik that there are shortcomings in current markers. Indeed, the reliability of sensory nerve conduction velocity (NCV) as the "gold standard" to detect SDN in children and adolescents with T1D has been questioned (2). When we assessed sensory NCV, sensory nerve action potential (SNAP) amplitude of the superficial peroneal and sural nerves, and compound muscle action potential (CMAP) scans of the peroneal nerve in young patients with T1D and age-matched healthy control subjects, we found that motor neuron damage may coincide with or even precede sensory damage. While sensory NCV did not differ significantly between patients (range 12.5–19.9 years) and control subjects, or between patients with well-controlled (duration <5 years, HbA_{1c} <8.0%) and poorly controlled (duration >10 years, HbA_{1c} >8.5%, and/or early signs of microvascular complications) T1D, SNAP amplitudes were lower in patients with poorly controlled T1D. Although diagnostic sensitivity was acceptable, accuracy and specificity were low (3).

CMAP scans revealed no difference in conventional motor nerve neurophysiological measures (axonal loss and reinnervation) between young T1D patients (range 8.08–23.58 years) and age-matched healthy control subjects (4). However, axonal excitability was significantly reduced in both well- and poorly controlled young patients and adults with T1D when compared with control subjects. This suggests that whereas early disturbances of motor neuronal function cannot be detected using conventional motor nerve neurophysiological measures, recently developed axonal excitability measures could prove useful in identifying the early signs of nerve function deterioration.

The abovementioned findings underscore the necessity for ongoing debate on appropriate surrogate measures. We caution against a singular focus on sensory nerves as our results indicate that (early) motor nerve dysfunction may also potentially be a suitable marker of SDN.

Duality of Interest. J.C.v.d.H. was supported by an unrestricted educational grant from Novo Nordisk. The authors received editorial support in the preparation of this text from Pim Dekker of Excerpta Medica, funded by Diabeter. No other potential conflicts of interest relevant to this article were reported.

References

1. Malik RA. Which test for diagnosing early human diabetic neuropathy? Diabetes 2014;63:2206–2208
2. Vinik A. Neuropathies in children and adolescents with diabetes: the tip of the iceberg. Pediatr Diabetes 2006;7:301–304
3. Van der Heyden J, van der Meer P, Birnie E, et al. Possibly promising methods in detecting early signs of peripheral diabetic neuropathy in young patients with type 1 diabetes mellitus. Pediatr Diabetes 2010;11(Suppl. 14):36
4. Van der Heyden J, van der Meer P, Birnie E, et al. Decreased excitability of the distal motor nerve of young patients with type 1 diabetes mellitus. Pediatr Diabetes 2013;14:519–525

[1]Diabeter, Center for Pediatric and Adolescent Diabetes Care and Research, Rotterdam, the Netherlands
[2]Department of Pediatric Endocrinology, Sophia Children's Hospital, Erasmus MC, University Medical Centre, Rotterdam, the Netherlands
[3]Department of Pediatrics, Sint Franciscus Gasthuis, Rotterdam, the Netherlands
[4]Institute of Health Policy & Management, Erasmus University Rotterdam, Rotterdam, the Netherlands
[5]Department of Clinical Neurophysiology, Erasmus MC, University Medical Centre, Rotterdam, the Netherlands

Corresponding author: Josine C. van der Heyden, j.vanderheyden@sfg.nl.