Journal of Iranian Medical Council, Volume 5, Issue no. 3
http://dx.doi.org/10.18502/jimc.v5i3.10939

Original Article

Comparing Screening Tools and Electrophysiological Findings of Sural and Peroneal Nerves in the Diagnosis of Neuropathy in Patients with Diabetes: A Cross-sectional Study

Hamid Reza Fateh[1,2], Mostafa Azimi[3] and Seyed Pezhman Madani[4]*

1. Department of Physical Medicine and Rehabilitation, Shariati Hospital, Tehran University of Medical Sciences (TUMS), Tehran, Iran

2. Diabetes Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

3. Sports Medicine Research Center, Neuroscience Institute, Tehran University of Medical Sciences, Tehran, Iran

4. Department of Physical Medicine and Rehabilitation, Neuromusculoskeletal Research Center, Iran University of Medical Sciences, Tehran, Iran

Abstract

Background: Some clinical scoring systems as the quantitative tools have been developed to assess the presence and severity of Diabetic Peripheral Neuropathy (DPN) based on both the patient's complaints and the physicians' findings. This study was aimed at assessing the presence and severity of sural and peroneal nerve neuropathies using Michigan Neuropathy Screening Instrument (MNSI) and United Kingdom Screening Test (UKST) questionnaire compared with electrodiagnosis assessments.

Methods: 148 patients with Diabetes Mellitus (DM) including 80 females and 68 males with a mean age of 57.6, 19 type 1DM and 129 type 2 DM were recruited in this study. The findings of the electrophysiological study such as peroneal and sural nerves' conduction delay, velocity and amplitude were gathered. The patients were also assessed regarding the clinical neuropathy status using the two instruments of MNSI and UK.

Results: The mean neuropathy score of MNSI and UKST were 2.2 (1.7) and 4.1 (3.0), respectively. Each instrument detected the DPN in 47.3% and 64.9% of the patients, respectively. Also, based on the nerve conduction studies (NCS), the neuropathy of sural and peroneal nerves was found in 54.1% and 79.7%, respectively. Unlike the peroneal nerve, there was a significant agreement between the electrodiagnosis assessment and the screening tools in the diagnosis of sural nerve neuropathy.

Conclusion: Given that NCS is a practical, simple, and non-invasive approach and also can determine the level of damage and regeneration in peripheral nerves, sural nerve conduction study is suggested as a convenient option for screening and diagnosing the diabetic neuropathy.

Keywords: Diabetes mellitus, Diabetic neuropathies, Electrodiagnosis, Michigan, Neural conduction, Peroneal nerve, Sural nerve, United Kingdom

*** Corresponding author**

Seyed Pezhman Madani, MD
Neuromusculoskeletal Research Center, Firoozgar Hospital, Tehran University of Medical Sciences, Tehran, Iran
Tel: +98 21 8214 1612
Fax: +98 21 8894 2970
Email: nmsrc@iums.ac.ir

Received: Aug 10 2021
Accepted: Oct 27 2021

Citation to this article:
Fateh HR, Azimi M, Madani SP. Comparing Screening Tools and Electrophysiological Findings of Sural and Peroneal Nerves in the Diagnosis of Neuropathy in Patients with Diabetes: A Cross-sectional Study. J Iran Med Counc. 2022;5(3):435-42.

Introduction

The most common complication of both type 1 Diabetes Mellitus (T1DM) and type 2 diabetes mellitus (T2DM) is neuropathy that is often neglected while it can increase the rate of hospitalizations, morbidities and mortalities of diabetes (1,2). This progressive complication can be very debilitating and affect people's quality of life severely (3-5). A decade ago, the global projection for the number of people who would be living with diabetes in 2025 was 438 million. But only after 5 years, 25 million has been added to that prediction (6). The incidence of polyneuropathy is associated with HbA1c levels and the duration of T2DM. Nevertheless, it may be present in the prediabetics and up to 18 percent of patients at the time of diagnosis. (7,8). In addition to various complications comprising imbalance, foot deformity and ulcers, fractures, and amputations, approximately one-third of diabetic patients with polyneuropathy suffer from neuropathic pain including burning, painful cold, electric shock, tingling, pins and needles, numbness, and itching in the hands and feet (9-11).

The diagnosis of Diabetic Peripheral Neuropathy (DPN) is based on the physician's clinical examination and patient's self-report, but almost half of DPNs are asymptomatic. As a result, using some questionnaires and electrodiagnosis tools can facilitate the detection process and help the management and prevention of the consequences in these cases. Michigan Neuropathy Screening Instrument (MNSI) (14,15) and United Kingdom screening test (UKST) (12,13,15) are objective and subjective questionnaires, respectively, and they are accurate, valid, and well-known in the diagnosis of diabetic neuropathy. NCS is also a non-invasive and precise method for diagnosing and determining the severity of neuropathy.

The main goal of the present study was to compare the effectiveness of sural and peroneal nerve conduction studies with the MNSI and UKST in confirming diabetic peripheral neuropathy.

Materials and Methods

This cross-sectional study was performed during 2016-19.

Sample size calculation

The prevalence of diabetic neuropathy is 81% on average (16) using the electrophysiological indicators of nerve conduction. Thus, considering p=0.71, Z=1.96, α=0.05, and d=0.07, the sample size was calculated 121.

148 known type I and II diabetes mellitus subjects were confirmed by endocrinologists with more than 18 years of age, both male and female with or without symptoms of neuropathy were comprised in this study. Patients with psychological problem, potential for peripheral neuropathy consisting of hereditary sensory neuropathy, vitamin B12 or folate deficiency, paraneoplastic diseases, autoimmune conditions, organs failure, hypothyroidism prolonged phenytoin or immunosuppressive drugs consumption, and ethanol abuse were excluded from the research (2,14). Besides assessing patients by MNSI, UKST, and Nerve Conduction Studies (NCS), the baseline characteristics including demographics, lipid profile, fasting blood sugar, disease duration, and history of diabetes-related complications were collected. Ethically each patient signed the informed consent form prior to participation in the study.

Instrument

United Kingdom Screening Test (UKST)

UKST is a simple, subjective, and symptom-based 9-score questionnaire composed of five questions about type, severity, and location of symptoms. Its cut-off point is ≥ 2 (17,18).

Michigan Neuropathy Screening Instrument (MNSI)

MNSI is an objective test to evaluate the history of neuropathic symptoms and physical examination to assess the sensation (ankle reflex and vibration) and appearance (deformities, dry skin, calluses, infections, fissures, and ulcer) of feet that is completed by an expert physician. The scores ≥ 2 are considered abnormal. Abnormality in each item gets grades 0.5 to 1 and at least more than 2 abnormal items is required to reach the score of neuropathy (19).

Electrophysiological assessment

NCS is the most suitable component of the electrophysiologic examination, as a valuable and fruitful tool which is intended as a gold standard test for verifying the neuropathy diagnosis. Patients

with one or more abnormal findings in amplitude, conduction velocity, and Distal Latency (DL) values were considered neuropathy (20–25). According to the previous studies, there is no general agreement on the criteria for polyneuropathy in NCS (21). Since DPN is a motor nerve of lower extremity and is more likely to be involved in neuropathy, we designed our study accordingly (24).

Bilateral peroneal nerve Compound Muscle Action Potentials (CMAPs) and sural nerve Sensory Nerve Action Potentials (SNAPs), Nerve Conduction Velocity (NCV), amplitude, and DL were carried out by a lecturer physiatrist by using 2-channel Oxford (Medelec-Synergy) electromyography instrument in a quiet room with proper ventilation condition. Normal values were considered based on the previous valid data (26). For peroneal nerve CMAP, the recording electrode was attached on the extensor digitorum brevis and peroneal nerve was stimulated distally at ankle, lateral to tibialis anterior tendon and proximally a few centimeters distal to the fibular head.

For sural nerve SNAP, the recording electrode was attached on the posterior aspect of the lateral malleolus and the stimulator was located 14 *cm* proximally in the posterior aspect of leg's midline (27).

Statistical analysis

Results were presented as mean ± standard deviation (SD) for quantitative variables and were summarized by frequency (percentage) for the categorical variables. Continuous variables were compared using T-test or Mann-Whitney U test whenever the data did not appear to have normal distribution or when the assumption of equal variances was violated across the study groups. Categorical variables were, on the other hand, compared using chi-square test. The data were analyzed using the IBM SPSS Statistics 24 (IBM Inc, New York, USA). p values of 0.05 or less were considered statistically significant.

Results

148 patients with diabetes mellitus were recruited in this study. Demographic characteristics of the patients were reported in table 1.

In the neuropathy evaluation, the mean score of MNSI (ranged 0 to 6) and UKST (ranged 0 to 9) were 2.2 (1.7) and 4.1 (3.0), respectively. According to the determined cut-off point in MNSI and UKST, peripheral neuropathy was detected in 47.3 and 64.9% of the patients, respectively. Also, based on NCS, the neuropathy of sural and peroneal nerves was found in 54.1 and 79.7%, respectively.

There was a strong correlation between the decrease in the sural amplitude and abnormality of both screening tools, the decrease in sural NCV and positive MNSI score, also, increasing peroneal nerve DL and NCV with neuropathy scores of MNSI and UKST (Table 2). Based on the UKST calcification, the severity of neuropathy in this study have been found mild (2–4): 20 (13.5%), moderate (5–6): 37 (25%) and severe (7–9): 39 (26.4 %).

Table 1. Baseline and general characteristics of the recruited patients

Variable	Frequency
Female/Male	80(54.1 %)/68(44 %)
Age	57.6 (11.4)*
DM1/DM2	19(12.8 %)/129(87.2%)
Duration of disease	9.9 (6.9)*
BMI	27.9 (4.2)*
HbA1c	8.0 (2.4)*
Total cholesterol	206.6 (36.9)*
LDL	120.4 (32.1)*
HDL	42.5 (11.0)*
Triglyceride	225.2 (124.1)*

*mean+/- standard deviation; BMI: Body Mass Index;

Table 2. Association of the MNSI and UK tools findings with the electrophysiological assessment

Electrophysiological assessment	Mean ± SD	MNSI tool		UK tool	
		R coefficient	p-value	R coefficient	p-value
Delayed conduction of Sural nerve (*ms*)	2.7 ± 0.4	-0.14	0.10	-0.05	0.51
Conduction amplitude of Sural nerve (*μv*)	12.1 ± 6.6	-0.37	0.001	-0.020	0.010
Conduction velocity of Sural nerve (*m/s*)	44.2 ± 7.3	-0.27	0.001	-0.15	0.070
Delayed conduction of peroneal nerve (*ms*)	5.2 ± 1.0	0.45	0.001	0.24	0.003
Conduction amplitude of peroneal nerve (*μv*)	1.8 ± 1.7	-0.16	0.04	-0.09	0.26
Conduction velocity of peroneal nerve (*m/s*)	40.4 ± 6.3	-0.38	0.001	-0.29	0.001

Table 3. Main determinants of diabetic neuropathy (p-values)

Predictor	MNSI tool	UK tool	NCS (sural)	NCS (peroneal)
Age > 50 y	0.01	0.41	0.01	0.98
Female gender	0.49	0.005	0.93	0.61
Duration > 10 y	0.003	0.030	0.07	0.76
HbA1c > 7%	0.13	0.28	0.44	0.68
TG > 200 *mg/dl*	0.68	0.22	0.21	0.45
CHOL > 240 *mg/dl*	0.85	0.30	0.63	0.29
HDL < 40 *mg/dl*	0.86	0.54	0.09	0.51
LDL > 160 *mg/dl*	0.15	0.66	0.22	0.24
BMI	0.59	0.40	0.35	0.051

Non-significant p values have been depicted in bold format; BMI: Body Mass Index;

This study showed a significant correlation between electrophysiological assessment and MNSI tool in the diagnosis of sural nerve neuropathy ($p<0.001$), however, this diagnostic correlation was not found between these two assessment tools in the detection of peroneal nerve neuropathy. Similarly, a correlation was found between electrophysiological assessment and the UK questionnaire in assessing sural nerve neuropathy ($p<0.001$), but not for diagnosing peroneal nerve neuropathy. In this regard, the MNSI questionnaire had a sensitivity of 74.2% and a specificity of 64.1% for diagnosing sural nerve neuropathy. Also, the sensitivity and specificity of the UK questionnaire for the diagnosis of this neuropathy were 80.0 and 69.2%, respectively. A strong correlation was revealed between the MNSI and UK total score (Pearson's correlation coefficient = 0.43, $p<0.001$) (Table 2).

Based on the MNSI questionnaire, the main determinants of diabetic neuropathy included age higher than 50 years ($p=0.010$) and disease duration longer than 10 years ($p=0.003$). Based on the UK questionnaire, female gender ($p=0.005$) and diabetes duration longer than 10 years ($p=0.030$) could predict the diabetic neuropathy. According to the electrophysiological assessment, age higher than 50 years was the major indicator for sural nerve neuropathy ($p=0.010$), whereas none of the baseline variables could predict peroneal nerve neuropathy (Table 3).

Discussion

Peripheral neuropathy is a common and important complication of diabetes with an overall prevalence of 45% (28), which can cause multiple disabilities. Therefore, early diagnosis and therapeutic interventions are essential (29), and as a result, various studies have been conducted over the years. Various methods have been evaluated and approved for the diagnosis of diabetic neuropathy, including clinical examinations, questionnaires, and electrophysiological tools, but due to difficulty in use and some shortcomings, there is still no suitable solution for early diagnosis of neuropathy (12-15). Neural conduction and electrodiagnostic studies have been suggested as potentially helpful tools to precisely assess peripheral neural function in these patients (30). In this regard, neural conduction studies have been accepted as a reliable, noninvasive comparative standard by which even mild sensory conductive abnormalities are diagnosed. Moreover, by the progression of diabetes, abnormal findings of peripheral nerve motor branches may also appear that can be easily diagnosed by EMG techniques (16). In a study conducted by Uluc *et al* (31), electrodiagnostic findings of the sural nerve were abnormal in 60% of the diabetic patients leading to well differentiation of those with neuropathy from other patients without this abnormality. Another study (32), revealed that the severity of peroneal nerve involvement could be diagnostically helpful when it is considered besides neurological clinical signs in the natural process of diabetic neuropathy. However, these diagnostic techniques, especially electromyography, may be technically challenging due to obesity, coldness of extremities, and need a complete assessment of the sensory-motor function of the multiple nerves in both upper and lower extremities (33).

During the last few years, some quantitative clinical scoring systems have been developed, such as the MNSI and the UK tools, to assess the presence and severity of diabetic neuropathy based on the patients' complaints and the physical findings. These tools had rapidly been used to screen patients for possible neuropathy due to their high sensitivity (47.3 and 64.9%, respectively), which is almost consistent with the sensitivity of the electrophysiological variables of the sural nerve (54.1%). This study showed a high sensitivity for both MNSI and UK tools to discover diabetic neuropathy. Also, there is a strong agreement between these tools to diagnose neuropathy. These two instruments can be applied as sensitive and applicable tools for early screening of diabetic neuropathy. However, due to their low specificity, requiring supplement tests and electrophysiological studies are also emphasized. Previous studies also pointed out that clinical tools such as the MNSI may not be entirely beneficial for diagnosing diabetic neuropathy. As shown by Uluc *et al* (31), electrodiagnostic findings of the sural nerve were abnormal in 60% of the diabetic patients leading to well differentiation of those with neuropathy from other patients without this abnormality. Our research showed that the diagnosis of neuropathy based on both MNSI and UK clinical tools agreed significantly with the electrophysiological diagnosis of the sural nerve neuropathy, but not with the peroneal nerve neuropathy that can be explained with high sensitivity of electrophysiological assessment of the peroneal nerve (79.7%). In fact, similar to the previous studies, electrophysiological assessment for diabetic neuropathy achieved higher sensitivity while considering peroneal nerve than the neuropathy detected by pure sural nerve assessment (34,35). It was also indicated by Negrin and Zara (32) that assessing the severity of peroneal nerve involvement can be diagnostically helpful when considered besides neurological clinical signs in the natural process of diabetic neuropathy. It seems that motor-fiber assessment of peroneal nerve can be helpful in cases of high suspicion of diabetic neuropathy without classic symptoms where mentioned tests are not positive.

Limitations

We did not evaluate asymptomatic diabetic patients in the form of a separate group and used limited objective tests such as Utah Early Neuropathy Scale and temperature threshold testing to assess diabetic neuropathy.

Discussion

Along with the sensitive screening instruments including MNSI and UKST, sural nerve NCS is a fruitful, objective, and simple approach in the diagnosis of diabetic neuropathy, and can complement the role of these questionnaires in the screening, confirming, and follow up of diabetic peripheral neuropathy.

Funding

This research had no funding source.

Disclosure

The authors had no conflict of interests to disclose.

References

1. Callaghan, BC, Price RS, Feldman EL. Distal symmetric polyneuropathy: a review. JAMA 2015 Nov 24;314(20):2172-81.

2. Fateh HR, Madani SP, Heshmat R, Larijani B. Correlation of Michigan neuropathy screening instrument, United Kingdom screening test and electrodiagnosis for early detection of diabetic peripheral neuropathy. J Diabetes Metab Disord 2016 Mar 25;15:8.

3. Nather A, Bee CS, Huak CY, Chew JLL, Lin CB, Neo S, et al. Epidemiology of diabetic foot problems and predictive factors for limb loss. J Diabetes Complications 2008 Mar-Apr;22(2):77-82.

4. Kioskli K, Scott W, Winkley K, Kylakos S, McCracken LM. Psychosocial factors in painful diabetic neuropathy: a systematic review of treatment trials and survey studies. Pain Med 2019 Sep 1;20(9):1756-73.

5. Fateh HR, Madani SP. Role of interdigital sensory nerve conduction study as a noninvasive approach for early diagnosis of diabetic peripheral neuropathy. J Diabetes Metab Disord 2021 Feb 15;20(1):71-75.

6. Diabetes Atlas. 9th edition. International Diabetes Federation; 2019.

7. Nisar MU, Asad A, Waqas A, Ali N, Nisar A, Qayyum MA, et al. Association of diabetic neuropathy with duration of type 2 diabetes and glycemic control. Cureus 2015 Aug 12; 7(8): e302.

8. Khalaf KM, Khudhair MS, Ashor AW. Vitamin B12 status and peripheral neuropathy in patients with type 2 diabetes mellitus. J Pak Med Assoc 2019 Aug;69(Suppl 3)(8):S40-S44.

9. Madani SP, Fateh HR, Forogh B, Fereshtehnejad SM, Ahadi T, Ghabousi P, et al. Validity and reliability of the Persian (Farsi) version of the DN4 (douleur neuropathique 4 questions) questionnaire for differential diagnosis of neuropathic from non-neuropathic pains. Pain Pract 2014 Jun;14(5):427-36.

10. Feldman EL, Callaghan BC, Pop-Busui R, Zochodne DW, Wright DE, Bennett DL, et al. Diabetic neuropathy. Nat Rev Dis Primers 2019 Jun 13;5(1):41.

11. Kobayashi M, Zochodne DW. Diabetic neuropathy and the sensory neuron: new aspects of pathogenesis and their treatment implications. J Diabetes Investig 2018 Nov;9(6):1239-1254.

12. Boulton AJM, Malik RA, Arezzo JC, Sosenko JM. Diabetic somatic neuropathies. Diabetes Care 2004 Jun;27(6):1458-86.

13. Vinik AI, Mehrabyan A. Diabetic neuropathies. Med Clin North Am 2004 Jul;88(4):947-99, xi.

14. Mete T, Aydin Y, Saka M, Cinar Yavuz H, Bilen S, Yalcin Y. Comparison of efficiencies of michigan neuropathy screening instrument, neurothesiometer, and electromyography for diagnosis of diabetic neuropathy. Int J Endocrinol 2013;2013:821745.

15. Farshchi A, Esteghamati A, Sari AA, Kebriaeezadeh A, Abdollahi M, Dorkoosh FA, et al. The cost of diabetes chronic complications among Iranian people with type 2 diabetes mellitus. J Diabetes Metab Disord 2014 Mar 4;13(1):42.

16. Lo YL, Xu LQ, Leoh TH, Dan YF, Tan YE, Nurjannah S, et al. Superficial peroneal sensory and sural nerve conduction studies in peripheral neuropathy. J Clin Neurosci 2006 Jun;13(5):547-9.

17. Oguejiofor OC, Odenigbo UC, Oguejiofor CBN. Screening For Peripheral Neuropathy In Diabetic Patients: The

benefits of the United Kingdom Screening Test (UKST). Trop J Med Res 2008;12(1):45–9.

18. Oguejiofor OC, Odenigbo CU, Oguejiofor CBN. Evaluation of the effect of duration of diabetes mellitus on peripheral neuropathy using the United Kingdom screening test scoring system, bio-thesiometry and aesthesiometry. Niger J Clin Pract 2010 Sep;13(3):240-7.

19. Herman WH, Pop-Busui R, Braffett BH, Martin CL, Cleary PA, Albers JW, et al. Use of the Michigan Neuropathy Screening Instrument as a measure of distal symmetrical peripheral neuropathy in Type 1 diabetes. Diabet Med 2012 Jul;29(7):937-44.

20. Kong X, Lesser EA, Potts FA, Gozani SN. Utilization of nerve conduction studies for the diagnosis of polyneuropathy in patients with diabetes: a retrospective analysis of a large patient series. J Diabetes Sci Technol 2008 Mar; 2(2):268–74.

21. England JD, Gronseth GS, Franklin G, Miller RG, Asbury AK, Carter GT, et al. Distal symmetric polyneuropathy: a definition for clinical research: report of the American academy of neurology, the American association of electrodiagnostic medicine, and the American academy of physical medicine and rehabilitation. Neurology 2005 Jan 25;64(2):199-207.

22. Daube JR. Electrophysiologic testing in diabetic neuropathy. In: Dyck P, Thomas P, editors. Diabetic Neuropathy. Philadelphia, PA: WB Saunders; 1999. p. 222–38.

23. Donofrio PD, Albers JW. AAEM minimonograph 34: polyneuropathy: classification by nerve conduction studies and electromyography. Muscle Nerve 1990 Oct;13(10):889-903.

24. Dyck PJ. Detection, characterization, and staging of polyneuropathy: assessed in diabetics. Muscle Nerve 1988 Jan;11(1):21-32.

25. Nasseri K, Strijers RL, Dekhuijzen LS, Buster M, Bertelsmann FW. Reproducibility of different methods for diagnosing and monitoring diabetic neuropathy. Electromyogr Clin Neurophysiol. 1998 Jul-Aug;38(5):295-9.

26. Kimura J. Electrodiagnosis in diseases of nerve and muscle, principles and practice, fourth edition: DPN. Appendix 1/ 4-5 tables/ 977–980 pp.

27. Dumitru D. Electrodiagnostic Medicine, chapter 5: nerve conduction studies. 2nd ed. Hanley & Belfus, INC; 2002. Part II; BASIC AND ADVANCED TECHNIQUES, chapter 5: nerve conduction studies. pp. 211–217.

28. Dyck PJ, Kratz KM, Karnes JL, Litchy WJ, Klein R, Pach JM. The revalence by staged severity of various types of diabetic neuropathy, and nephropathy, in population-based cohort. Neurology 1993 Apr;43(4):817-24.

29. An JY, Park MS, Kim JS, Shon YM, Lee SJ, Kim YI, et al. Comparison of diabetic neuropathy symptom score and medial plantar sensory nerve conduction studies in diabetic patients showing normal routine nerve conduction studies. Intern Med 2008;47(15):1395-8.

30. Bril V, Ellison R, Ngo M, Bergstrom B, Raynard D, Gin H. Electrophysiological monitoring in clinical trials. Roche Neuropathy Study Group. Muscle Nerve 1998 Nov;21(11):1368-73.

31. Uluc K, Isak B, Borucu D, Temucin CM, Cetinkaya Y, Koytak PK, et al. Medial plantar and dorsal sural nerve conduction studies increase the sensitivity in the detection of neuropathy in diabetic patients. Clin Neurophysiol 2008 Apr;119(4):880-5.

32. Negrin P, Zara G. Conduction studies as prognostic parameters in the natural history of diabetic neuropathy: a long-term follow-up of 114 patients. Electromyogr Clin Neurophysiol 1995 Oct;35(6):341-50.

33. Moghtaderi A, Bakhshipour A, Rashidi H. Validation of Michigan neuropathy screening instrument for diabetic peripheral neuropathy. Clin Neurol Neurosurg. 2006 Jul;108(5):477-81.

34. Hussain G, Rizvi SAA, Singhal S, Zubair M, Ahmad J. Cross sectional study to evaluate the effect of duration of type 2 diabetes mellitus on the nerveconduction velocity in diabetic peripheral neuropathy. Diabetes Metab Syndr 2014 Jan-Mar;8(1):48-52.

35. Hyllienmark L, Alstrand N, Jonsson B, Ludvigsson J, Cooray G, Wahlberg-Topp J. Early electrophysiological abnormalities and clinical neuropathy: a prospective study in patients with type 1 diabetes. Diabetes Care 2013 Oct;36(10):3187-94.