

# Evaluation of sural nerve automated nerve conduction study in the diagnosis of peripheral neuropathy in patients with type 2 diabetes mellitus

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## Abstract

**Introduction:** New tests for improved diagnosis of diabetic peripheral neuropathy (DPN) are useful.

**Material and methods:** We evaluated the utility of automated nerve conduction study (NCS) of the sural nerve with a new portable device for the diagnosis of DPN in patients with type 2 diabetes mellitus (T2DM). This study included 114 T2DM patients (58 men) with mean age  $64.60 \pm 8.61$  years. Exclusion criteria were B<sub>12</sub> depletion, alcohol abuse and other causes of peripheral neuropathy. The reference method was the Neuropathy Disability Score (NDS) with a threshold  $NDS \geq 3$ . Sural nerve automated NCS was carried out with the portable NC-stat DPNCheck device. Sensory nerve conduction velocity and sensory nerve action potential amplitude were measured bilaterally. Automated NCS was considered abnormal when  $\geq 1$  of the two aforementioned neurophysiological parameters was abnormal in at least one leg.

**Results:** Examination with NC-stat DPNCheck exhibited 90.48% sensitivity, 86.11% specificity, 79.17% positive predictive value (PPV) and 93.94% negative predictive value (NPV). The positive likelihood ratio (LR+) was 6.51 and the negative likelihood ratio (LR-) was 0.11.

**Conclusions:** Sural nerve automated NCS with the NC-stat DPNCheck device exhibits high sensitivity and specificity for the diagnosis of DPN in T2DM.

**Key words:** diabetes mellitus, diabetic neuropathy, diagnosis, nerve conduction study.

## Introduction

The abundance of new tests for diabetic peripheral neuropathy (DPN) suggests that there is a poorly met need to improve its diagnosis in everyday reality [1–3]. Some of these new tests are more suitable as screening tools, while others are appropriate for patient evaluation and follow-up in specialised centres [1–3]. Among the former, the indicator test Neuropad has been shown to exhibit a high sensitivity and negative predictive value as a screening tool for DPN [4–6]. A further approach to improve diagnosis includes automated nerve conduction study (NCS), which can be easily and quickly performed without specialised personnel [7, 8]. The first devices for automated NCS harboured a pre-arranged series of electrodes permitting automatic selection of the clearest electrical

signal [7, 8]. With such devices, automated NCS was found to yield high sensitivity and specificity compared to established classical NCS [8]. More recently, a new, even simpler device has become commercially available, which offers automated NCS specifically of the sural nerve: the NC-stat DPNCheck (NeuroMetrix, Inc., Waltham, MA) [9]. This can be used by health care professionals after < 60 min training, and the examination takes approximately 2 min. A small study has shown that NC-stat DPNCheck yields high sensitivity and specificity in comparison with classical NCS, despite some slight over-estimation of nerve conduction velocity [9]. Importantly, very good intra- and inter-observer reproducibility for this examination has already been demonstrated [9, 10].

However, NC-stat DPNCheck has not been compared with standardised clinical examination. This comparison is useful, because traditional NCS is not widely available, in contrast to clinical examination [11, 12]. Given that NC-stat DPNCheck appears even simpler and can be used by diabetes nurses as well, we aimed to examine the diagnostic performance of this new device against standardised clinical examination for the diagnosis of DPN in patients with type 2 diabetes mellitus (T2DM).

## Material and methods

This study included 114 T2DM patients (58 men, 56 women) who attended the Diabetes Clinic of the Second Department of Internal Medicine at Democritus University of Thrace, Greece. An age- and sex-matched group of 46 healthy controls (24 men, 22 women) was also included. The study was approved by the local institutional ethics committee and patients gave their informed consent.

Diagnosis of DPN was based on clinical examination by the standardised neuropathy disability score (NDS), according to Young *et al.* [11]. This evaluates ankle reflexes, as well as vibration, pain and temperature perception on the feet bilaterally [11], and is an established measure of the presence and severity of DPN [12]. An NDS  $\geq 3$  was considered diagnostic of DPN [11, 12]. Exclusion criteria were B<sub>12</sub> depletion, alcohol abuse, lumbar spine disorders and other causes of peripheral neuropathy.

Examination with NC-stat DPNCheck was carried out at constant room temperature (20–25°C) as follows (Figure 1). Patients lay in the supine position and both sural nerves were examined. The device harbours two stimulating probes, a biosensor, a display screen, a button, and a battery. The probes were first immersed in gel to improve electrical conductance. The bigger probe was located by the examiner on the lateral side of the ankle in the middle of the lateral malleolus, and the biosensor was located in a straight line on the calf.

Pressing the button, the examiner could choose the right or left limb and start measurements. On the display screen, sensory nerve conduction amplitude (SNAP) and sensory nerve conduction velocity (SNCV) were shown. Two measurements were performed in each limb, and the mean value of measured parameters was calculated. Automated NCS was considered abnormal when SNAP was < 4  $\mu$ V in at least one leg and/or SNCV was < 40 m/s in at least one leg [13]. The examiner was blinded to the clinical NDS data.

Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of automated NCS against NDS were calculated by standard formulae. Data were expressed as mean  $\pm$  SD. Continuous variables were compared by *t*-test. Likelihood ratios and Youden's J were calculated by standard formulae [14].

## Results

Patient age was 64.60  $\pm$  8.61 years. Diabetic peripheral neuropathy was diagnosed in 42 (36.84%) patients by NDS. Patients with DPN had insignificantly higher age than those without DPN (66.40  $\pm$  8.96 vs. 63.56  $\pm$  8.29 years, *p* = 0.089), as well as significantly longer diabetes duration (16.14  $\pm$  7.28 vs. 11.82  $\pm$  7.89 years, *p* = 0.004) and higher glycated haemoglobin (HbA<sub>1c</sub>) (8.90  $\pm$  1.30 vs. 7.20  $\pm$  1.30%, *p* < 0.001).

In T2DM patients, examination with NC-stat DPNCheck exhibited 90.48% sensitivity and 86.11% specificity (Table I). The positive likelihood ratio (LR+) was 6.51 and the negative likelihood ratio (LR-) was 0.11. Youden's J was 0.77.

In the control group, age was 64.19  $\pm$  8.82 years. The NDS was normal in all subjects, while automated NCS was abnormal in two subjects.

## Discussion

To the best of our knowledge, this is the first study examining the diagnostic performance of



Figure 1. Examination with the NC-stat DPNCheck device

**Table I.** Diagnostic performance of automated NCS vs. clinical examination (NDS)

Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	LR+	LR-	Youden's J
90.48	86.11	79.17	93.94	6.51	0.11	0.77

LR+: positive likelihood ratio, LR-: negative likelihood ratio, NCS – nerve conduction study, NDS – neuropathy disability score, NPV – negative predictive value, PPV – positive predictive value.

automated NCS by the NC-stat DPNCheck device against standardised clinical examination. It was found that NC-stat DPNCheck exhibited a very good diagnostic performance, as reflected in the high Youden's J. Its sensitivity and NPV were excellent, and its specificity and PPV were high. In particular, its LR+ was good [14], suggesting that a positive result is of value in ruling in DPN. Most importantly, its LR- was very low, indicating that the test is especially reliable as a screening tool to rule out DPN.

Lee *et al.* [9] recently demonstrated generally small differences in electrophysiological parameters between NC-stat DPNCheck and classical NCS. Against the latter, sensitivity and specificity of the former were: 88% and 94%, respectively for SNAP; 94% and 82%, respectively for SNCV; 95% and 71%, respectively for  $\geq 1$  abnormal electrophysiological parameter [9]. These data are very important in the validation of measurements with the new device. Although their study addressed a different question from ours, the findings of the two works together provide evidence for the diagnostic utility of the new test.

The practical implications of our findings are that the new automated NCS device merits further use in everyday clinical practice. In an endeavour to simplify classical NCS, we have previously shown that the sural sensory/radial motor amplitude ratio has high diagnostic sensitivity compared with the complete neurophysiological examination, but it is less time-demanding, thereby having the potential to enable examination of more patients [15]. NC-stat DPNCheck is a step further ahead: its application may be expected to increase patient examination rates for DPN, which remains a priority in order to reduce diabetic foot morbidity [16, 17]. Indeed, the new test may be used by diabetes nurses and other health care professionals after minimal training. Therefore, NC-stat DPNCheck may be widely employed as a screening tool, with particular value in exclusion of DPN. A disadvantage is, certainly, the cost for purchase of the device and disposable biosensor electrodes, so a cost-utility analysis should be designed.

The strengths of the present study are the inclusion of a relatively adequate patient series, the use of the established NDS, the simple, straightforward neurophysiological criteria permitting widespread use of the new device as a screening tool, and the clear message. Its limitations may

be outlined as follows. First, we included patients from a tertiary care setting, and therefore the results may not be directly applicable to the general diabetic population. A second limitation may be that we did not confirm the diagnosis of DPN by classical NCS. However, this was beyond the scope of our study. Instead, we chose to compare the new device with standardised clinical examination, which is more widely available. For this purpose, we used the established NDS [6, 11, 12]. Finally, we only studied patients with T2DM, and so more experience with type 1 diabetes is needed.

In conclusion, the findings of this study suggest that sural nerve automated NCS with the NC-stat DPNCheck device exhibits high sensitivity and specificity for the diagnosis of clinical DPN in T2DM. This high diagnostic performance suggests that the test may prove useful as a screening tool of DPN, with a particular utility in exclusion of this condition. The present results add to the increasing appreciation of the importance that automated NCS may have in improving diagnosis of DPN, including the primary health care setting [7–10]. In view of the need to increase our knowledge in DPN [17–19], they encourage further use of the new device in clinical practice.

### Conflicts of interest

Nikolaos Papanas has served as a member in the scientific advisory board of TrigoCare International, distributor of Neuropad.

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