Diagnostic Performance of Sural Nerve Conduction Amplitude is Maintained in the Elderly

Xuan Kong, PhD, Bonniejean Boettcher, MS, Kenneth Snow, MD, MBA, Shai N. Gozani, MD, PhD, NeuroMetrix, Inc, *Waltham, MA*

OBJECTIVE

The objective of this study was to evaluate the hypothesis that the diagnostic performance of sural amplitude is age independent.

BACKGROUND

The clinical detection of diabetic peripheral neuropathy (DPN) in the elderly is challenging because of normal age related nerve degeneration that leads to false positives, such as with vibratory sensation testing. Sural nerve conduction amplitude is a sensitive and specific biomarker for DPN, which has recently become available as a point-of-care test.

METHODS AND MATERIALS

The study was a retrospective cross-sectional comparison of sural amplitude in two population-based cohorts. The normal cohort consisted of 527 subjects without clinical evidence of DPN. The diabetes cohort consisted of 1091 subjects, primarily with Type 2 diabetes, extracted from a data registry (77 contributing clinics). All measurements were obtained using identical methodology. The cohorts were divided into three age matched groups (<45, 45-64, ≥65 years). In each group, the area under the ROC curve served as a measure of diagnostic performance. Quantile regression on the sample median (50th percentile) was performed to determine age dependence of sural amplitude for each cohort. The 95th percentile confidence intervals of regression slope were based on 500 bootstrap sample datasets with equal nerve count from each age group.

RESULTS

The sural amplitude decreased from the youngest to oldest age groups in both cohorts (42% in normal, 67% in diabetes).

The rate of sural amplitude decrease with age was similar in both groups at 2.1µV (95%CI: [-0.26, -0.16]) per decade in the normal group and 1.6µV (95%CI: [-0.19, -0.14]) per decade in the diabetes group (see Figure 1)

Sural amplitude discrimination in the ≥65 group was only slightly worse than the 45-64 group (0.85 vs. 0.88) and better than the <45 group (0.85 vs. 0.77). (see Table 1)
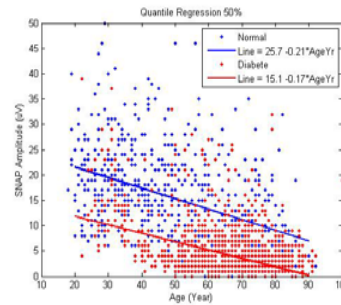
Figure 1.

Table 1.

Age (Years)	Normal Amplitude in Microvolts (N)	Diabetes Amplitude in Microvolts (N)	ROC (95% CI)
< 45	19.7 ± 8.2 (257)	12.0 ± 7.8 (107)	0.77 (0.71 – 0.83)
45-64	16.2 ± 8.0 (155)	5.8 ± 5.8 (324)	0.88 (0.85 – 0.91)
≥65	11.5 ± 7.6 (115)	4.0 ± 4.5 (660)	0.85 (0.81 – 0.88)

Study Limitations

Limitations of this study include a lack of information on duration of diabetes as well as glycemic control in the diabetic cohort. In addition, the distribution of subjects was biased with a higher percentage of diabetic subjects in the oldest age group compared to the youngest. This issue was taken into account through the use of bootstrapping in calculating the slopes of amplitude-age relationship and the 95th percentile confidence intervals.

CONCLUSIONS

Our analysis suggests that the age-related rate of sural nerve amplitude decline is statistically similar in the non-diabetic and diabetic age groups, and therefore it appears that diabetes represents an incremental loss of nerve fibers over and above normal aging.

Further, because the rate of change in sural nerve amplitude is similar in both diabetic and non-diabetic subjects, the discrimination between the two cohorts is similar across all age groups as evidenced by the comparable ROC values. The small differences in ROC values could be due to differences in prevalence of diabetes in the three cohorts.

This study demonstrates that although diabetes compounds normal age related nerve degeneration, measurement of sural nerve amplitude enables evaluation of nerve function in all age groups.