Comparison of Sudomotor and Sensory Nerve Testing in Painful Sensory Neuropathies

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Abstract

Objective: To compare results of quantitative sudomotor axon reflex testing (QSART), dorsal sural, and sural sensory nerve testing in patients with painful sensory neuropathy (PSN).

Methods: Fifty-six patients with symptoms and neurologic examinations consistent with PSN who had both autonomic and nerve conduction studies were identified from 376 patients with a clinical diagnosis of painful neuropathy. Cases were clinically categorized as large-fiber or small-fiber neuropathies by described criteria. The results of sural, dorsal sural, and QSART tests were then analyzed in relationship to these two clinical groups.

Results: Evidence of unmyelinated fiber abnormalities by QSART was noted in 85% of clinical large-fiber and 69% of clinical small-fiber groups. Dorsal sural potentials were absent in all the large-fiber group but also in 52% of clinically classified small-fiber neuropathies. When QSART and dorsal sural abnormalities were combined, the identification of abnormalities in all the cases of PSN was 89% with 75% of cases (42) showing mixed large and small fiber abnormalities, 14% unmyelinated sensory fiber abnormalities (by QSART), and 11% normal studies.

Conclusion: This study demonstrates the value of combining both QSART and dorsal sural sensory testing in verifying the diagnosis of PSN. The majority of cases demonstrate involvement of unmyelinated C fibers as well as large/medium myelinated fibers, thereby separating mixed large- and small-fiber sensory neuropathies from those cases classified by clinical criteria solely as small-fiber neuropathy.

Key Words: painful sensory neuropathy, quantitative sudomotor axon reflex testing, small-fiber neuropathy, large-fiber neuropathy, and dorsal sural nerve

INTRODUCTION

Painful sensory neuropathies (PSN) comprise a clinical group of peripheral neuropathies defined by their symptomatology and findings. The cause of the pain is presumed to be the result of abnormalities of the unmyelinated C fibers that can be isolated or in combination with large sensory fiber abnormalities. Results of electrodiagnostic testing including sural sensory testing are often normal in many of these cases.

The purpose of this study was to evaluate the sensitivities of sural and dorsal sural sensory conductions and quantitative sudomotor axon reflex testing (QSART) in the detection and classification of PSN. A number of noninvasive special tests are available for detecting sensory neuropathies, and a range of sensitivities has been reported.1,2 QSART is used to establish the existence of unmyelinated small-fiber dysfunction.3-5 This test measures sweat production locally in the skin by iontophoresis of acetylcholine and thus assesses the integrity of small sympathetic cholinergic fibers with the sensitivity to detect PSN at 73%6 and to detect small-fiber neuropathy (SFN) between 60% and 80%.2 Abnormal sural sensory potentials have been used as an indicator of large-fiber sensory nerve pathology.7 When sural sensory study results are normal, bilateral assessment of the
dorsal sural sensory potentials increases the detection of large-fiber peripheral neuropathy by evaluating the medium and small distal branches of the sural nerve.  

MATERIALS AND METHODS

Three hundred seventy-six neuropathy patients who had both autonomic function testing and nerve conduction studies performed in the Baylor College of Medicine neurology laboratories from 2005 to 2009 were identified. Fifty-six patients (30 males and 26 females; age range, 20–80 years) were identified whose symptoms (burning pins and needles, prickling, electric shocks, or shooting pains) were compatible with PSN. The etiology noted in these cases was idiopathic in 31 (56%), diabetic in 13 (23%), and mixed other etiologies in 12 (21%). Patients with lumbosacral radiculopathies or sciatica were excluded.

From these 56 patients with PSN, cases were then classified by clinical criteria into large-fiber or small-fiber categories. Twenty-nine patients were isolated whose cases fulfilled the clinical criteria of Stewart et al for SFN.

Any of the following neurologic abnormalities were accepted as indicative of SFN: reduced or absent pinprick sensation in the feet, reduced response to light touch in the distal feet, reduced or absent vibratory sensation in the toes, and reduced or absent ankle reflexes with other reflexes normal.

Typical painful distal sensory symptoms with a normal sensory and motor examination were also considered compatible with SFN. Patients with one or more of the following were classified as having large-fiber neuropathies: any loss of proprioception, reduced vibratory sensation at or above the ankles, any distal wasting or weakness, or loss of reflexes above the ankles. Cases with abnormal bilateral motor conduction velocities in the legs were also excluded. We then compared the QSART, dorsal sural, and sural sensory testing results in these two clinical groups of small- and large-fiber sensory neuropathies.

Dorsal sural and sural sensory testing and QSART were performed according to described methods. In keeping with the findings from our previous study, the bilateral dorsal sural sensory potentials were evaluated and listed as normal (greater than 4 μV) or absent. The minimum normal amplitude of the sural potential was 5 μV, and the sensory velocity was 35 m/s or greater. We listed the QSART responses as normal (sudomotor subscore of zero) or abnormal (sudomotor subscore of 1–3 inclusive). We did not include patients who had a “hung-up” response on QSART. Although this response may occur in a dying-back peripheral neuropathy, it is not specific and may occur with axonal regeneration. For this reason, we only included abnormal QSART responses that indicated decreased sweat production at the foot or a length-dependent pattern of abnormal sweat production.

To compare the sensitivities of two diagnostic tests, we used McNair’s test. This is a test appropriate to the situation in which the two tests will be compared on the same sample of patients. The Pearson chi-square test statistic was used to compare two observed proportions from independent samples defined by large-fiber and small-fiber status. Statistical significance was assessed at the 0.05 level. To measure the degree of agreement between QSART and dorsal sural tests, we used Cohen’s kappa (κ) statistic. The statistical analysis software package R was used to perform all data analyses.

RESULTS

Table 1 reports the results of the sensory nerve action potentials and QSART testing in 56 patients with PSN subdivided clinically into small- and large-fiber neuropathies. Forty-two (75%) of all patients had abnormal dorsal sural potentials, 15 in the group classified as small fiber. Forty-three of both groups of patients (77%) had abnormal QSART findings, 20 in the small-fiber group. In the small-fiber group, eight had abnormal QSART (14%) and six had...
normal QSART results (11%). Sural, dorsal sural, and QSART testing results were normal in six of the 56 (11%) with PSN.

Table 2 reports the sensitivities in the same group of 56 patients. We considered two types of comparisons: QSART versus dorsal sural and large-fiber versus small-fiber group. Among all patients (small- and large-fiber categories), QSART was 77% (43 of 56) sensitive and dorsal sural testing was 75% sensitive (42 of 56). There was no significant difference between QSART and dorsal sural testing sensitivities ($P = 1$). When restricted to the small-fiber group, QSART was 69% sensitive and dorsal sural testing was 52% ($P = 0.13$). When restricted to large-fiber cases, QSART sensitivity was 85% and dorsal sural was 100% ($P = 0.046$). We also considered the sensitivity as defined by using either test, that is, the percentage of patients for whom at least one of the tests—QSART or dorsal sural—was a true positive (Table 2). Among all patients, the combined approach led to a sensitivity of 89%.

When restricted to small- and large-fiber groups, sensitivity was 79% and 100%, respectively. Comparing the combined sensitivity of QSART and dorsal sural tests, we found: 1) among small-fiber classifications, the combined testing gives a significantly ($P = 0.005$) higher sensitivity (79%) than the dorsal sural (52%); 2) among large-fiber cases, the combined testing gives a significantly ($P = 0.046$) higher sensitivity (100%) than the QSART (85%); 3) among all patients, the combined testing gives a significantly ($P < 0.01$) higher sensitivity than either test alone. The agreement between QSART and dorsal sural in all patients was calculated as $\kappa = 0.26$, which indicates fair agreement between the two tests.$^{10}$ Similar agreement was observed in the small-fiber classification ($\kappa = 0.23$). The sensitivity of the dorsal sural test was significantly ($P = 0.0001$) higher in large-fiber (100%) compared with the small-fiber group (52%). QSART was statistically equally sensitive ($P = 0.26$) in large fiber (85%) and small fiber (69%).

### TABLE 1. Comparison of Sensory Nerve Action Potentials and Sudomotor Testing in 56 Cases Clinically Classified as Small- and Large-Fiber Painful Sensory Neuropathies

<table>
<thead>
<tr>
<th>Results</th>
<th>Clinical Small Fiber (n = 29)</th>
<th>Clinical Large Fiber (n = 27)</th>
<th>Combined Total (n = 56)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sural and Dorsal Sural: Normal</td>
<td>6 (21%)</td>
<td>3 (10%)</td>
<td>4 (15%)</td>
</tr>
<tr>
<td>Sural: Normal; Dorsal Sural: Abnormal</td>
<td>8 (28%)</td>
<td>12 (41%)</td>
<td>23 (85%)</td>
</tr>
</tbody>
</table>

Percentages are relative to sample sizes shown in column headings.

QSART, quantitative sudomotor axon reflex testing.

### TABLE 2. Sensitivity of QSART and Dorsal Sural Testing in Small- and Large-Fiber Painful Sensory Neuropathies

<table>
<thead>
<tr>
<th>Test</th>
<th>Clinical Small Fiber (n = 29)</th>
<th>Clinical Large Fiber (n = 27)</th>
<th>Combined Total (n = 56)</th>
</tr>
</thead>
<tbody>
<tr>
<td>QSART</td>
<td>20 (69%)</td>
<td>23 (85%)</td>
<td>43 (77%)</td>
</tr>
<tr>
<td>Dorsal sural</td>
<td>15 (52%)</td>
<td>27 (100%)</td>
<td>42 (75%)</td>
</tr>
<tr>
<td>QSART and dorsal sural</td>
<td>23 (79%)</td>
<td>27 (100%)</td>
<td>50 (89%)</td>
</tr>
</tbody>
</table>

Percentages are relative to sample sizes shown in column headings.

QSART, quantitative sudomotor axon reflex testing.
**DISCUSSION**

Pain is a predominant symptom in patients with SFN and usually has a burning, pricking, or shock-like characteristic. In our patient group, 33 (59%) described their pain as burning, and the remainder (41%) described their symptoms as shooting, pricking, or shock-like electric sensations.

Clinical evaluation of patients with the symptoms of PSN involves demonstration of objective signs of neuropathy and then classifying them into small- or large-fiber type. However, examination is often normal or provides only minimal neurologic findings of neuropathy. Electrodiagnostic methods have also been limited in demonstrating abnormalities and categorizing large- and small-fiber neuropathies. The presence of typical neuropathic pain in PSN indicates the involvement of small unmyelinated C fibers or myelinated A delta fibers. Autonomic symptoms may be present clinically, but sudomotor testing is required to demonstrate objective abnormalities of unmyelinated fibers. The results of sural sensory testing in PSN are often normal, but when they are abnormal, they indicate large-fiber involvement. Dorsal sural testing improves sensitivity in neuropathies when the sural conduction studies are normal.

The results in this study in 56 patients with PSN show the unpredictability of test results when the cases are artificially separated into large- and small-fiber neuropathies by clinical criteria. The QSART is sensitive in both large- (85%) and small-fiber (69%) classifications (Table 2). Because QSART evaluates unmyelinated small C fibers, these findings confirm that unmyelinated small-fiber pathology accounts for the pain in the majority of clinical large-fiber PSN, and these cases should be classified as mixed large- and small-fiber neuropathies. Similarly, Oh et al found evidence of large-fiber dysfunction in 65 of 100 patients with predominantly SFN by proximal near nerve needle recordings of the plantar nerve.

Although criteria such as those of Stewart et al are generally accepted, they have never been validated. These findings indicate these criteria are not strict enough to exclude many patients with mixed painful neuropathies caused by the combined involvement of large myelinated and small unmyelinated fibers.

The clinical group classified as SFN had QSART abnormalities in 20 of 29 cases (69%); however, absent dorsal sural potentials were noted in 52% of those same cases, indicating that distal small or medium myelinated fibers are also involved and changing the classification to a mixed-fiber neuropathy.

Diagnosing SFN is recognized as a challenging clinical problem. Among several alternative diagnostic tools, skin biopsy has been reported to be a good procedure for diagnosing SFN. Reporting on three different tests in SFN, Devigili et al found that the skin biopsy had the highest sensitivity, specificity, and positive and negative predictive values. Their data on 67 cases show sensitivities of 88%, 62.6%, and 56.7% comparing skin biopsy, clinical examination, and quantitative sensory testing. They did not perform QSART testing to confirm unmyelinated fiber abnormalities and only sural sensory conduction testing was done. Because skin biopsy evaluates only unmyelinated small nerve fibers and not myelinated small and large fibers, skin biopsy results alone do not exclude a mixed sensory fiber neuropathy in these cases.

This study demonstrates the mixed fiber-type pathology in the majority of PSN classified by clinical features as large-fiber myelinated or small-fiber unmyelinated neuropathies. Both small-fiber and large-fiber clinical groups show combinations of unmyelinated and myelinated pathophysiology with a small subgroup demonstrating unmyelinated small-fiber abnormalities by QSART testing (14%).

**REFERENCES**


