Moisture Status of the Skin of the Feet Assessed by the Visual Test Neuropad Correlates With Foot Ulceration in Diabetes

CHRISTINA VOULGARI, MD
NICHOLAS TENTOLOURIS, MD

OBJECTIVE — To examine the association between the moisture status of the skin of the feet with foot ulceration in subjects with diabetes.

RESEARCH DESIGN AND METHODS — A total of 379 subjects with diabetes were examined. Assessment of peripheral neuropathy was based on neuropathy symptom score, neuropathy disability score, vibration perception threshold, and the 10-g monofilament perception. The moisture status of the skin of the feet was assessed using the visual test Neuropad.

RESULTS — Patients with foot ulceration had more severe peripheral neuropathy and more often an abnormal Neuropad response. Multivariate logistic regression analysis demonstrated that the odds of foot ulceration increased with measures of neuropathy but increased also with an abnormal Neuropad response.

CONCLUSIONS — An abnormal Neuropad response correlates with foot ulceration in subjects with diabetes. This finding, if confirmed prospectively, suggests that the Neuropad test may be included in the screening tests for the prediction of foot ulceration.

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ARTICLE

Damage of the peripheral sympathetic nerves results in sudomotor dysfunction, which manifests as dry skin of the feet and may result in callus and/or fissure formation and eventually in foot ulceration (1,2). The American Diabetes Association recommends examination of sudomotor function for the detection of diabetic neuropathies (3); however, the lack of specific equipment has restricted the study of sudomotor function and its contribution to foot ulceration. The Neuropad test (miro Verbandstoffe, Wiehl-Drabenderhohe, Germany) is a novel visual test for the assessment of the moisture status of the skin of the feet (4,5). The research hypothesis we tested herein was that an abnormal Neuropad response may be associated with foot ulceration in subjects with diabetes.

RESEARCH DESIGN AND METHODS — A total of 379 adult subjects were recruited in this study. Exclusion criteria were age 75 years, ankle-brachial pressure index 0.9. Differences between the studied groups were tested using parametric or nonparametric methods according to the specific indications, whereas a χ² test was used to compare categorical data. Univariate and multivariate logistic regression analyses (stepwise backward method) were performed to look for associations between the studied parameters with foot ulceration. The area under the receiver operating characteristic (ROC) curve of various established risk factors for foot ulceration and of the Neuropad test was calculated. The area under the ROC curve indicates how informative a test for the prediction of foot ulceration is. P values 0.05 were considered statistically significant.

RESULTS — Subjects with foot ulceration were mostly men and had longer diabetes duration, worse glycemic control, and more often peripheral neuropathy and peripheral artery disease than subjects without foot ulceration. The values of the NSS, NDS, and VPT were higher, whereas monofilament insensitization and an abnormal Neuropad result were more often documented in patients...
Table 1—Demographic and clinical characteristics as well as the association [odds ratio (95% CI)] between the studied parameters with foot ulceration

| Without foot ulceration | With foot ulceration | P      |
|-------------------------|----------------------|--------|
| n                       | 258                  | 121    | —     |
| Age (years)             | 60.0 ± 11.7          | 63.2 ± 10.2 | 0.86  |
| Male/female [n (%)]     | 130 (50.4)/128 (49.6)| 84 (69.4)/37 (30.6) | 0.001 |
| Type 1/type 2 diabetes [n (%)] | 15 (5.8)/243 (94.2) | 8 (6.6)/113 (93.4) | 0.46  |
| Duration of diabetes (years) [median value (IQR)] | 10.0 (5.0–16.0) | 18.0 (10.0–25.0) | <0.001 |
| A1C (%)                 | 7.4 ± 1.6            | 9.2 ± 2.4 | <0.001 |
| VPT (V)                 | 21.5 ± 11.6          | 37.4 ± 12.2 | <0.001 |
| VPT ≥25 V [n (%)]       | 85 (32.9)            | 101 (83.5) | <0.001 |
| NSS [median value (IQR)] | 4.5 (0.0–6.0)      | 6.0 (4.0–7.0) | <0.001 |
| NDS [median value (IQR)] | 2.0 (0.0–5.0)     | 7.0 (6.0–10.0) | <0.001 |
| NDS ≥6 [n (%)]          | 62 (24.0)            | 92 (76.0) | <0.001 |
| Monofilament insensation [n (%)] | 36 (14.0)    | 70 (57.9) | <0.001 |
| Neuropathy [n (%)]      | 114 (44.2)           | 114 (94.2) | <0.001 |
| Ankle-brachial pressure index | 1.00 ± 0.22      | 0.98 ± 0.22 | 0.050 |
| Peripheral artery disease [n (%)] | 42 (16.3)     | 31 (25.6) | 0.09  |
| Abnormal Neuropad result [n (%)] | 135 (52.3)   | 115 (95.0) | <0.001 |

Univariate analysis

- Age (1 year) OR 1.00, 95% CI 0.98–1.02, P = 0.56
- Sex (male vs. female) OR 1.83, 95% CI 1.14–2.95, P = 0.01
- Duration of diabetes (1 year) OR 1.08, 95% CI 1.05–1.11, P < 0.001
- A1C (1%) OR 1.32, 95% CI 1.18–1.74, P = 0.002
- NSS (1 unit) OR 1.24, 95% CI 1.13–1.36, P < 0.001
- NDS (1 unit) OR 1.61, 95% CI 1.45–1.79, P < 0.001
- NDS ≥6 vs. <6 OR 10.7, 95% CI 6.25–18.40, P < 0.001
- VPT (1 V) OR 1.10, 95% CI 1.08–1.13, P < 0.001
- VPT ≥25 vs. <25 V OR 12.23, 95% CI 6.20–22.68, P < 0.001
- Monofilament result (insensation vs. sensation) OR 8.33, 95% CI 4.18–16.59, P < 0.001
- Neuropad result (abnormal vs. normal) OR 17.3, 95% CI 7.36–40.8, P < 0.001
- Peripheral artery disease (yes vs. no) OR 1.84, 95% CI 1.07–3.10, P = 0.02

Multivariate analysis*

- Model 1
  - NDS ≥6 vs. <6 OR 6.70, 95% CI 3.31–13.35, P < 0.001
- Model 2
  - VPT ≥25 vs. <25 V OR 11.91, 95% CI 6.03–21.86, P < 0.001
- Model 3
  - Monofilament result (insensation vs. sensation) OR 6.40, 95% CI 3.09–13.28, P < 0.001
- Model 4
  - Neuropad result (abnormal vs. normal) OR 16.28, 95% CI 6.27–38.24, P < 0.001

Data are means ± SD unless otherwise indicated. IQR, interquartile range. Sex, NDS ≥6 vs. <6, VPT ≥25 vs. <25 V, monofilament result (insensation vs. sensation), Neuropad result (abnormal vs. normal), and peripheral artery disease (yes vs. no) were analyzed as categorical variables; all the other variables were analyzed as continuous variables in both univariate and multivariate analysis. *Each one of the models 1–4 were adjusted in addition for age, sex, duration of diabetes, A1C, NSS, and peripheral artery disease status.

with foot ulceration (Table 1). The Neuropad result was not different between patients with neuropathic and neuroischemic ulcers (P = 0.30).

Univariate logistic regression analysis showed that the odds of foot ulceration increased with male sex; longer duration of diabetes; worse diabetes control; increasing NSS, NDS, and VPT; monofilament insensation; presence of peripheral artery disease; and abnormal Neuropad response. Multivariate logistic regression analysis after adjustment for age, sex, duration of diabetes, A1C, NSS, and peripheral artery disease status demonstrated that the odds of foot ulceration increased with higher NDS, VPT, and monofilament insensation as well as with an abnormal Neuropad result (Table 1).

The area (± SE) under the ROC curve for the identification of patients with foot ulceration of VPT ≥25 vs. <25 V was 0.76 ± 0.02 (P < 0.001; sensitivity 85.4%; specificity 67.6%), of NDS ≥6 vs. <6 was 0.76 ± 0.02 (P < 0.001; sensitivity 75.7%; specificity 77.8%), of monofilament result (insensation vs. sensation) was 0.72 ± 0.03 (P < 0.001; sensitivity 57.4%; specificity 86.3%), and of the Neuropad result (abnormal vs. normal) was 0.71 ± 0.03 (P < 0.001; sensitivity 97.1%; specificity 49.3%). The area under the ROC curve of Neuropad testing did not differ significantly from that of VPT, NDS, and monofilament examination. No adverse events were observed from the Neuropad use.

CONCLUSIONS—This study has shown that dryness of the skin of the feet correlates with foot ulceration. Subclinical sudomotor dysfunction can be de-
Dry skin and foot ulceration
tected early in diabetes, even in subjects
with normal nerve conduction velocities (9). We showed that dryness of the skin of
the feet was detected in 95% of the pa-
tients with foot ulceration using the Neu-
ropad test. These findings agree with
previous data showing sudomotor dys-
function assessed with the sympathetic
skin response in the vast majority of pa-
tients with foot ulceration (10).
Noteworthy, the comparison of the
values of the areas under the ROC curves
demonstrated that the results obtained by
Neuropad testing are as informative as those obtained by determination of other
neurological modalities commonly used
for the prediction of foot ulceration such
as VPT, NDS, and monofilament testing.
Identification of patients at risk for
foot ulceration using simple and reliable
methods is of clinical relevance. The
American Diabetes Association recom-
mends the combined use of simple tests
including pinprick, temperature, vibra-
tion, and 10-g monofilament perception
as well as ankle reflexes for this purpose
(11). Our findings suggest that the Neu-
ropad can be included in the screening tests
for the prediction of foot ulceration. Advan-
tages of the Neuropad are its simplicity,
wide availability, high performance for the
diagnosis of peripheral neuropathy, and
high reproducibility (5,12). Moreover, the
test can be self-performed and evaluated
safely by the patients (13).
This is a cross-sectional study and a
casual relationship between the moisture
status of the skin of the feet, and foot ulc-
eration cannot be established. Moreover,
although the odds ratio is large, suggesting
that there is an association between an ab-
normal Neuropad response and foot ulc-
eration, the CIs are wide, and it is necessary
to be cautious about the interpretation of the
finding.
In summary, dryness of the skin of
the feet assessed by the Neuropad test cor-
relates with foot ulceration. This finding,
if confirmed prospectively, suggests that the Neuropad may be included in the
screening tests for the prediction of foot ulceration in subjects with diabetes.

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