

Underdiagnosis of Peripheral Neuropathy in Type 2 Diabetes

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Diabetic peripheral neuropathy and its late sequelae cost >\$4 billion annually in the U.S. (1). Improved glycemic control, early detection, and preventive care can prevent or delay adverse outcomes (2–4). An annual foot exam, which may include monofilament testing, is recommended by the American Diabetes Association (5). Unfortunately, neuropathy screening is underutilized in primary care practice (6,7). The GOAL A1C (Glycemic Optimization with Algorithms and Labs At Point of Care) study assessed methods of A1C testing and insulin titration monitoring strategies in a large nationwide sample of predominantly primary care patients with type 2 diabetes. At baseline, physician perception of the presence of neuropathy was assessed via a survey before monofilament testing. A comparison between physician perception and monofilament testing is reported.

RESEARCH DESIGN AND METHODS

GOAL A1C was a randomized, open-label, parallel, four-arm study that compared the impact of point of care versus laboratory A1C testing and weekly versus less frequent insulin titration monitoring on glycemic control in patients with type 2 diabetes adding insulin glargine to existing oral antidiabetic therapy. Eligible patients were aged ≥ 18 years, inadequately controlled on oral antidiabetic agents (A1C >7.0%), and can-

didates for insulin. All signed informed consent and were randomized.

During the pretreatment phase, physician perception of neuropathy was assessed: physicians responded “yes” or “no” (without prompting) to a survey question, “Does subject have or has (this subject) had clinically significant neuropathy?” Monofilament testing was then conducted by the same physician.

Two monofilaments (3.61 and 5.07) were used. Before testing, patients felt the monofilament on their hands. During testing, monofilaments were applied (each up to three times) in random sequence to the plantar surface of the great toe on one foot with enough force to bend the monofilament. With eyes closed, patients indicated when a touch occurred. Results were scored as follows: no neuropathy = feels both monofilaments, mild/moderate = feels the 5.07 but not the 3.61 monofilament, severe (insensate foot) = unable to feel either monofilament, and nonsense result = feels the 3.61 but not the 5.07 monofilament.

Comparisons of baseline patient characteristics and neuropathy were performed with ANOVA (continuous variables) and χ^2 tests (categorical variables). Explanatory effects of characteristics on neuropathy type were explored using logistic regression with backward selection. Comparison of correct diagnoses between endocrinologists and nonendocrinologists was performed with a Cochran-

Mantel-Haenszel test, stratifying by neuropathy type.

RESULTS— There were 7,892 patients enrolled from 2,142 U.S. sites. Baseline data were available for 7,378 patients (93.5%). Mean age was 57 years, duration of diabetes was 8 years, and average baseline A1C was 8.9%. Physicians reported an 18% prevalence of neuropathy. Subsequent monofilament testing detected no neuropathy in 63%, mild/moderate neuropathy in 30%, and severe neuropathy in 7% of patients. Physician perception and monofilament testing were concordant in 14% of patients ($n = 1,042$).

Physicians prospectively identified only 31 and 66% of patients with mild/moderate and severe neuropathy, respectively (Table 1). Nonendocrinologists (90% of investigators; $n = 2,297$) correctly identified mild/moderate and severe neuropathy in 31 and 64% of patients, respectively. Endocrine specialists (10% of investigators; $n = 258$) correctly identified mild/moderate and severe neuropathy in 36 and 74% of patients, respectively ($P < 0.0001$ for correct diagnoses by endocrinologists compared with nonendocrinologists).

By regression analysis, aged ≥ 50 years (odds ratio [OR] 1.58), male sex (OR 1.17), diabetes duration >7 years (OR 1.29), feeling “pins and needles” (OR 2.91), history of foot ulcers (OR 5.20), and height ≥ 1.7 m (OR 1.43) were significantly associated with neuropathy ($P = 0.0440$ for male sex; $P < 0.0001$ for other characteristics). Weight and A1C level were not associated with neuropathy. Patients with severe neuropathy were more likely to report experiencing feelings of “pins and needles,” a history of foot ulcers, and being prescribed custom footwear than were patients with mild/moderate neuropathy or no neuropathy.

CONCLUSIONS— Monofilament testing is a simple noninvasive independent predictor of risk for foot lesions (8,9). Monofilament testing detected a 37% prevalence of neuropathy in patients with type 2 diabetes in our large nation-

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A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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Table 1—Comparison of point-of-care monofilament testing and clinical diagnosis of neuropathy (n = 7,378)

Monofilament diagnosis		Physician perception	
		No neuropathy	Neuropathy
No neuropathy	4,628 (63)	4,304 (93)*	324 (7)
Mild/moderate neuropathy	2,209 (30)	1,524 (69)	685 (31)*
Severe neuropathy	541 (7)	184 (34)	357 (66)*

Data are n (%). *Indicates concordant diagnoses. Overall concordance 5,346/7,378 (72%).

wide sample, which is more than twice the prevalence identified by physicians before testing. Physicians detected a greater proportion of severe neuropathy than mild/moderate neuropathy.

Despite the established relationship between glycemic control and neuropathy (4,10), we did not identify A1C as a risk factor. Use of a single A1C measurement and exclusion of patients with A1C <7.0% could have masked an association (9).

Our study had a number of limitations. Definitive diagnostic studies to confirm neuropathy were not conducted. We employed a nonstandard protocol for monofilament testing but used it to minimize variability among the >2,000 investigators who participated. Restricting testing to one side may have favored inclusion of some cases of secondary mononeuropathy unrelated to diabetes. Testing the dorsum of the big toe or testing multiple sites (8,11) might have increased sensitivity. It is important to consider, however, that single-site screening may be more feasible in busy clinical practice and appears to improve detection.

Overall, physicians underestimate neuropathy in many patients with type 2 diabetes who are under their care and thus may be missing potential opportuni-

ties for early intervention. Systematic monofilament testing can facilitate earlier diagnosis and appropriate preventive care to reduce adverse outcomes.

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