Methods used in the tracking of Diabetic Neuropathy: an integrative review

Métodos utilizados no rastreamento da Neuropatia Diabética: uma revisão integrativa

Métodos utilizados en el seguimiento de la Neuropatía Diabética: una revisión integrativa

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RESUMO

Objetivo: Identificar os principais métodos de rastreamento utilizados na detecção da neuropatia em pacientes com Diabetes Mellitus tipo 2. Método: Revisão integrativa de literatura realizada entre julho e dezembro de 2023 em quatro bases de dados (Pubmed, MEDLINE, LILACS e BDENF). Resultados: Identificou-se 23 métodos diagnósticos, dos quais 21,7% avaliaram fibras finas, 43,4% fibras grossas e 34,7% ambas as fibras. O Monofilamento 10g destaca-se como o método mais utilizado, presente em 52,9% dos estudos, seguido do Sudoscan 35,2%, contudo o padrão ouro para diagnostico da neuropatia diabética é o estudo de condução nervosa, sendo a detecção precoce um desafio. Conclusão: No diagnóstico da neuropatia diabética é indispensável o rastreamento combinado com teste de diagnóstico, devendo-se testar minimamente o reflexo do tornozelo, a sensação térmica e a vibratória para manter uma boa acurácia diagnóstica, sendo que instrumentos objetivos podem favorecer e padronizar a identificação da neuropatia diabética.

Descritores: Diabetes Mellitus; Enfermagem; Neuropatias Diabéticas; Estudo de Avaliação.

ABSTRACT

Objective: Identify the main tracking methods used in the detection of neuropathy in patients with Type 2 Diabetes Mellitus. Method: Integrative literature review conducted between July and December 2023 in four databases (Pubmed, MEDLINE, LILACS, and BDENF). Results: Twenty-three diagnostic methods were identified, of which 21.7% assessed small fibers, 43.4% assessed large fibers, and 34.7% assessed both types of fibers. The 10g Monofilament stands out as the most used method, present in 52.9% of the studies, followed by Sudoscan at 35.2%. However, the gold standard for diagnosing diabetic neuropathy is the nerve conduction study, with early detection being a challenge. Conclusion: In the diagnosis of diabetic neuropathy, combined screening combined with diagnostic testing is essential. It is necessary to test at least the ankle reflex, thermal sensation, and vibratory sensation to maintain good diagnostic accuracy. Objective instruments can favor and standardize the identification of diabetic neuropathy.

Descriptors: Diabetes Mellitus; Nursing; Diabetic Neuropathies; Evaluation Study.

RESUMEN

Objetivo: Identificar los principales métodos de rastreo utilizados en la detección de la neuropatía en pacientes con Diabetes Mellitus tipo 2. Método: Revisión integrativa de la literatura realizada entre julio y diciembre de 2023 en cuatro bases de datos (Pubmed, MEDLINE, LILACS y BDENF). Resultados: Se identificaron veintitrés métodos diagnósticos, de los cuales el 21,7% evaluaron fibras finas, el 43,4% fibras gruesas y el 34,7% ambas fibras. El Monofilamento de 10g se destaca como el método más utilizado, presente en el 52,9% de los estudios, seguido del Sudoscan con un 35,2%. Sin embargo, el estándar de oro para el diagnóstico de la neuropatía diabética es el estudio de conducción nerviosa, siendo la detección precoz un desafío. Conclusión: En el diagnóstico de la neuropatía diabética, el rastreo combinado es essencial el cribado combinado com pruebas diagnóstica. Se debe probar al menos el reflejo del tobillo, la sensación térmica y la vibratoria para mantener una buena precisión diagnóstica. Los instrumentos objetivos pueden favorecer y estandarizar la identificación de la neuropatía diabética.

Descriptores: Diabetes Mellitus; Enfermería; Neuropatías Diabéticas; Estudio de Evaluación.

REVISÃO

Introduction

Diabetes Mellitus (DM) is defined as a chronic metabolic disorder of multifactorial origin, characterized by prolonged hyperglycemia, and its classification is based on etiopathogenesis. Type 2 Diabetes Mellitus (T2DM), an insidious and progressive subtype, is more common among the adult population and is associated with insulin resistance resulting from dietary habits, lifestyle, and aging.[1]

According to the 2021 annual atlas of the International Diabetes Federation (IDF), approximately 537 million adults aged between 20 and 79 years live with DM worldwide, generating healthcare expenditures exceeding 966 billion dollars. In Brazil, it affects approximately 15.8 million people. Complications associated with DM may be acute (hypoglycemia, hyperosmolar hyperglycemic state, and diabetic ketoacidosis) or chronic, both microvascular and macrovascular (such as retinopathy, nephropathy, peripheral neuropathy, peripheral vascular disease, cerebrovascular disease, and coronary artery disease).[2–3]

Among the microvascular complications, Diabetic Neuropathy (DN) stands out. It is characterized by diffuse and progressive lesions in the lower limbs (LLs), triggered by vascular/ischemic and/or neurological alterations resulting from persistent hyperglycemia. Around 50% of patients develop DN at some point during their clinical course, especially after 10 years. Moreover, DN may be followed by ulcers and infection, producing physiological and anatomical distortion. Signs and symptoms are subdivided into sensory (skin discomfort, tingling, prickling sensation, stinging, and hyper- or hypoesthesia), motor (impaired coordination and motor skills, weakness, imbalance, paralysis, and altered gait), and/or autonomic (hot skin, dry or excessively sweaty).[3–6]

The Brazilian Diabetes Society (SBD, 2024) recommends that all patients undergo DN screening at the time of T2DM diagnosis. If the test results are negative, it is suggested that the screening be repeated annually.[16] The 10g monofilament is the most commonly used method for assessing protective sensation, the 128Hz tuning fork for vibration testing, the pin for pain evaluation, cotton for tactile testing, and the reflex hammer for reflex assessment.[7]

In this context, DN has been investigated from various perspectives, either in isolation or in combination with other tests. These studies are conducted both in primary healthcare and in hospital settings. In this scenario, considering the variety of studies, there is a growing focus on identifying the best strategies for early detection of DN, given that DM is a disease of high global prevalence and that late diagnosis is associated with ulcerative complications, amputations, and increased morbidity and mortality. It is therefore crucial for the nursing team to be involved in promptly identifying neuropathy and delaying complications arising from the progression of DM.[6] Accordingly, this study aims to identify the main screening methods used in the detection of neuropathy in patients with Type 2 Diabetes Mellitus.

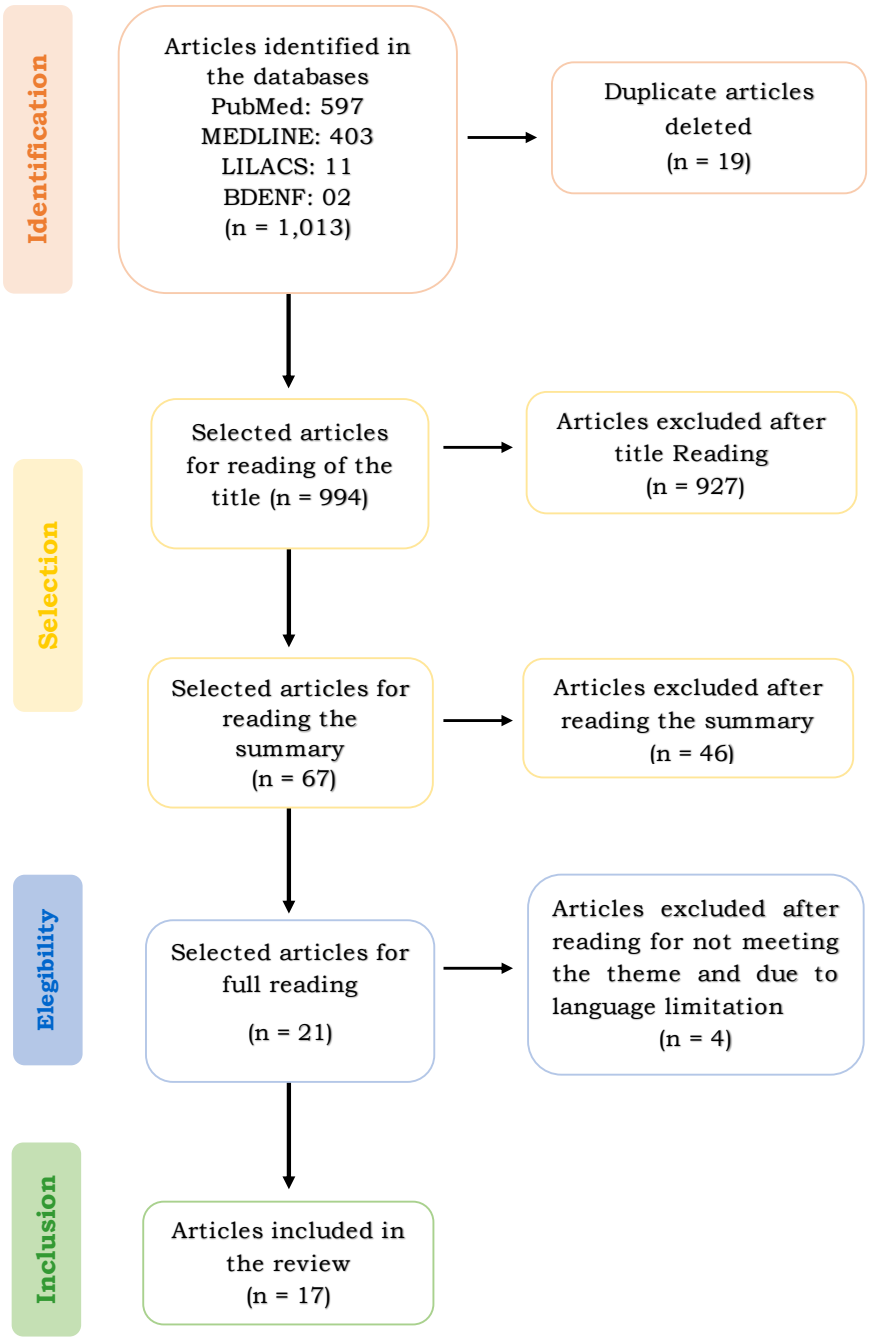
Methodology

This is an integrative literature review (ILR), a systematic model that provides scientific rigor and is divided into six stages: 1) identification of the topic and selection of the hypothesis, 2) literature search and sampling, 3) data extraction/categorization, 4) analysis of the included studies, 5) interpretation, and 6) data synthesis.[8] This research was conducted between July and December 2023 using the databases of the U.S. National Library of Medicine National Institutes of Health (PubMed) and the Virtual Health Library (VHL), including Medical Literature Analysis and Retrieval System Online (MEDLINE), Latin American and Caribbean Literature on Health Sciences (LILACS), and the Nursing Database (BDENF). The descriptors used were terms listed in the Health Sciences Descriptors (DeCS) and the Medical Subject Headings (MeSH), in both Portuguese and English.

Figure 1 shows the flowchart of the article selection process for this review. The initial sample consisted of 597 articles found in the PubMed database, 403 in MEDLINE, 11 in LILACS, and 2 in BDENF, totaling 1,013 articles. Of these, 19 were excluded due to duplication. After reading the titles, 927 were excluded for not addressing the chosen topic. Sixty-seven articles were selected for abstract reading, of which 46 were excluded for not meeting the established criteria. Twenty-one articles were read in full, and 4 were not selected due to not meeting the inclusion criteria and/or language limitations (2 articles available only in Chinese could not be read or translated). After this selection process, 17 articles were included in the present ILR.

For article eligibility, the inclusion criteria were clinical trials, screening and diagnostic studies on peripheral diabetic neuropathy, available in full and with no language restrictions. Additionally, studies involving adults aged ≥ 18 years with a diagnosis of T2DM, conducted between 2013 and 2023, were included. The exclusion criteria were systematic reviews, studies involving animals or pediatric/adolescent participants, studies with a total or majority sample of participants with type 1 diabetes (T1DM), other types of diabetic neuropathy, and materials published before the ten-year timeframe (2013–2023). In this ILR, the PICo search strategy was adopted, whose acronym stands for P – population/problem/patient, I – interest, and Co – context; defined as follows P–Patients diagnosed with T2DM; I – Undergoing screening methods for diabetic neuropathy; Co – Assessed in primary care, outpatient clinics, and specialized centers to identify and understand the effectiveness and types of tests used. From this, the guiding research question was derived: "What are the screening methods for diabetic neuropathy in patients with T2DM?"[8–9]

Figure 1- Flowchart of the methodological trajectory based on PRISMA guidelines. Brasília, 2024.



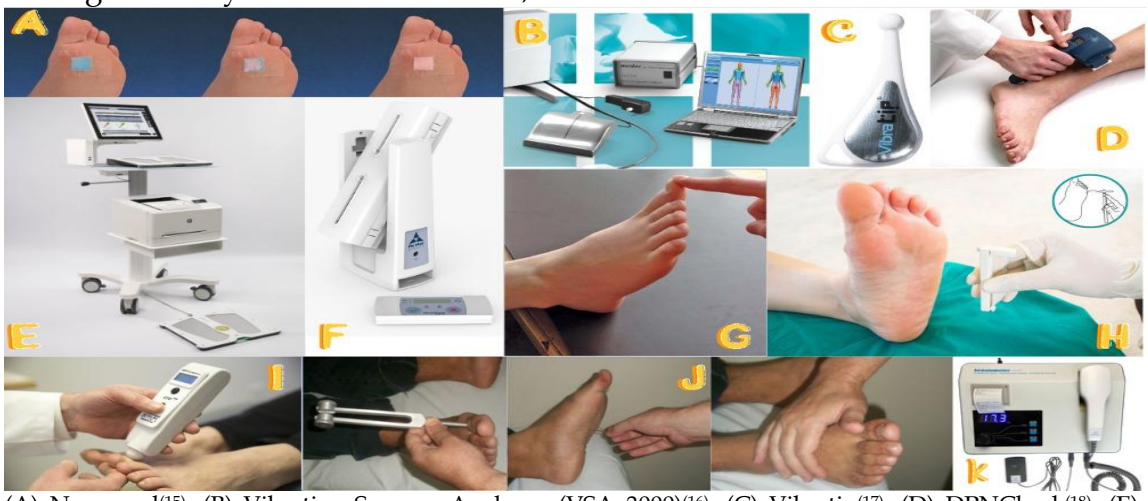
To identify the tests reviewed in this study, we opted to present how they relate to the analysis of nerve fibers. Screening and diagnostic tests for diabetic neuropathy (DN) can be categorized based on the type of nerve fiber analyzed. These are stratified by thickness and nerve conduction according to the Erlanger and Gasser Classification, in which type A fibers (α – alpha, β – beta, γ – gamma, and *δ* – delta) are the thickest and most myelinated, while type C fibers are thinner and unmyelinated. It is known that DN initially affects the unmyelinated autonomic small fibers (type C), followed by the lightly myelinated sensory fibers (type A*δ*), and eventually degenerates into damage of the thick, myelinated motor fibers (types Aα and Aβ), resulting in the characteristic symptomatology of DN.[10]

Results

A total of 17 articles written in English were included in the review. Of these, one was conducted in Austria (5.8%), four in China (23.5%), one in South Korea (5.8%), two in the United States (11.7%), one in Greece (5.8%), two in Mexico (11.7%), three in the United Kingdom (17.6%), one in Brazil (5.8%), and two in Pakistan (11.7%).

Table I presents 23 distinct diagnostic methods identified in the studies, of which 21.7% assessed small fibers, 43.4% large fibers, and 34.7% both types together. Regarding small fibers, the identified tests were: Neuropad, NerveCheck, Corneal Confocal Microscopy, Intraepidermal Nerve Fiber Biopsy, and Sudoscan. The tests that assessed large fibers were: Monofilament Test, Ipswich Touch Test, DPNCheck, 128Hz Tuning Fork, 128Hz ETF Prototype, Pressure Specified Sensory Device (PSSD), Vibratip, Nerve Conduction Studies (NCS), Biothesiometer, and Neurothesiometer. The Neuropathy Disability Score (NDS), Quantitative Sensory Testing (QST), VSA-3000, Michigan Neuropathy Screening Instrument (MNSI), Toronto Consensus Criteria, Neuropathy Symptom Score (NSS), Norfolk Quality of Life-Diabetic Neuropathy (QOL-DN), and Diabetic Neuropathy Examination and Diabetic Neuropathy Symptom Score (DNE and DNS) assessed both fiber types together. Figure 2 contains images of the tests.

Figure 2- Examples of tests used in the evaluation of Diabetic Neuropathy (DN) among the analyzed studies. Brasília, 2024.



(A) Neuropad[15]; (B) Vibration Sensory Analyzer (VSA–3000)[16]; (C) Vibratip[17]; (D) DPNCheck[18]; (E) Sudoscan Equipment(19); (F) NerveCheck[20]; (G) Ipswich Touch Test(21); (H) 10g Monofilament[22]; (I) 128 Hz Electronic Tuning Fork (ETF)[23]; (J) Physical examination and neuropathy disability score (NDS)[24]; (K) Biothesiometer[25].

The painful characteristics of diabetic neuropathy (DN) were evaluated and described directly in two studies: the first using the McGill Pain Questionnaire[11] and the second through self-reports and descriptions of symptoms by the participants.[12] Among the 161 participants evaluated, 93 had DN+ (present) and described the quality of lower limb pain as numbness (32.3%) and burning/stinging (29.4%), with reports of worsening symptoms at night. Among the 34 patients with DN– (absent), 45.6% were asymptomatic, while 41.7% complained of burning sensations in the feet.[12] According to the

studies, the clinical profile of patients with DN+ compared to those without diagnosed neuropathy is characterized by older age, longer duration of diabetes, poorer glycemic control (elevated HbA1c), and impaired pancreatic function. Additionally, smoking was found to be associated with greater sudomotor dysfunction, indicating severe nerve damage and contributing to the progression and prevalence of microvascular complications in patients with T2DM.[13-17]

Chart I. Presentation of the analyzed articles included in the integrative review and division by instruments of the neuropathy analysis. Brasilia, 2024.

	Authors	Year	Number of participants	Diagnosis/Screening Methods	Average time to diagnose DM (in years)	Complementary evaluations
1.	Manes C, Papanas N, Exiara T, Katsiki N, Papantoniou S, Kirlaki E, et al.	2014	569 ND- / 441 ND+ n = 1.010	Neuropad	10,5 ND- 14,4 ND+	----
2.	O'Brien T, Karem J	2014	18 ND- / 37 ND+ n = 55	128Hz ETF, MF10g, biothesiometer and clear discrimination test	----	----
3.	Sharma S, Kerry C, Atkins H, Rayman G	2014	*** ND- / *** ND+ n = 331	Ipswich Touch Test e MF10g	----	----
4.	Khan FF, Numan A, Khawaja KI, Atif A, Fatima A, Masud F	2015	72 ND- / 38 ND+ n = 110	DNS and DNE	5,3 ND+	HbA1c
5.	Ruhdorfer AS, Azaryan M, Kraus J, Grinzinger S, Hitzl W, Ebmer J, et al.	2015	*** ND- / *** ND+ n = 55	PSSD, MF10g and NCS	12,2 em média	HbA1c; IMC;
6.	Arshad AR, Alvi KY	2016	68 ND- / 93 ND+ n = 161	MF10g, Digital Biotensiometer, ankle reflexes, and 128Hz tuning fork	3 ND- 6 ND+	HbA1c; BMI; Diastolic Blood Pressure; Systolic Blood Pressure; Fasting Blood Glucose
7.	Mao F, Liu S, Qiao X, Zheng H, Xiong Q, Wen J et al.	2016	258 ND- / 89 ND+ n = 347	Sudoscan, NSS and NDS	6 ND– 9 ND+ asymptomatic 11 ND+ symptomatic	HbA1c; BMI; BP; Dyslipidemia; Alcoholism; Smoking; Waist and hip circumference
8.	Ponirakis G, Odriozola MN, Odriozola S, Petropoulos IN, Azmi S, Ferdousi M, et al.	2016	41 ND- / 33 ND+ 70 controles sem DM n = 144	NerveCheck, NCS, Corneal Microscopy and Biopsy of the intraepidermal fiber density	23,3 ND- 37,6 ND+	HbA1c; IMC; PAS; Colesterol
9.	Zhao Z, Ji L,	2016	1496 ND- /	AR+PP+T+V+P	----	----

	Zheng L, Yang L, Yuan H, Chen L, et al.		2387 ND+ n = 3.883			
10.	Azzopardi K, Gatt A, Chockalingam N, Formosa C	2017	71 without dysfunction / 29 with dysfunctionn = 100	Vibratip, tuning fork 128Hz and neurotester	19,53 on avergae	HbA1c; BMI; Smoking; Daily medications
11.	Brown JJ, Pribesh SL, Baskette KG, Vinik AI, Colberg SR	2017	7 ND- / 27 ND+ n = 34	MF10g, DPNCheck, questionário QOL-DN e diapasão 128Hz	----	HbA1c; IMC
12.	Jin J, Wang W, Gu T, Chen W, Lu J, Bi Y, et al.	2017	120 ND- / 60 ND+ n = 180	Sudoscan, AR+PP+T+V+P e NCS	8,4 ND- 13,1 ND+	HbA1c; BMI; Fasting and postprandial C-peptide; Fasting blood sugar
13.	Santos TRM, Melo JV, Leite NC, Salles GF, Cardoso CRL	2018	258 ND- / 168 ND+ n = 426	VSA-3000, NSS, NDS and MF10g	6 ND- 10 ND+	HbA1c; BMI; Fasting Glucose; Serum Creatinine; Albuminuria; Aortic Stiffness; Cholesterol; Vitamin B12
14.	Carbajal-Ramírez A, Hernández-Domínguez JA, Molina-Ayala MA, Rojas-Uribe MM, Chávez-Negrete A	2019	134 without dysfunction / 87 with dysfunctionn = 221	Sudoscan, MNSI and NCS	> 5 and <5 ND+	IMC
15.	García-Ulloa AC, Almeda-Valdes P, Cuatecontzi-Xochitiotzi TE, Ramírez-García JA, Díaz-Pineda M, Garnica-Carrillo F, et al.	2022	1620 without dysfunction / 619 with dysfunctionn = 2,243	Sudoscan and NCS	< 5 ND+	HbA1c; BMI; DBP; SBP; HR; Cholesterol; Triglycerides; Kidney function test; Uric Acid
16.	Lin K, Wu Y, Liu S, Huang J, Chen G, Zeng Q	2022	188 ND- / 327 ND+ n = 515	Sudoscan and NCS	7,7 ND- 8,8 ND+	HbA1c; BMI; Lipid profile; Alcoholism; Smoking; Kidney function test; Myocardial infarction; Stroke
17.	Oh TJ, Song Y, Jang HC, Choi SH	2022	104 ND- / 40 ND+ n = 144	Sudoscan, MNSI, NCS and MF10g	9,5 ND- 9,5 ND+	HbA1c; BMI; Fasting blood sugar; Lipid profile; Kidney function test

*** Information not specified in the study; ---- Data not evaluated by the study; AR – Ankle Reflex Assessment; AVE – Stroke; DM – Diabetes Mellitus; DNE – Diabetic Neuropathy Examination; DNS – Diabetic Neuropathy Symptom; ETF – Electronic Tuning Fork Prototype; FC – Heart Rate; HAS – Systemic Arterial Hypertension; HbA1c – Glycated Hemoglobin; IAM – Acute Myocardial Infarction; IMC – Body Mass Index; MF10g – Monofilament 10g; MNSI – Michigan Neuropathy Screening Instrument; ND– – Absent Diabetic Neuropathy; ND+ – Present Diabetic Neuropathy; NDS – Neuropathy Disability Score; NCS – Nerve Conduction Study; NSS – Neuropathy Symptom Score; P – Pressure Perception Assessment with Monofilament 10g; PAD – Diastolic Blood Pressure; PAS – Systolic Blood Pressure; PP – Assessment of Pinprick Sensation; PSSD – Specified Pressure Sensory Device; QOL-DN – Norfolk Quality of Life-Diabetic Neuropathy; T – Assessment of Thermal Sensation with the Tip Therm; TSH – Thyroid

Stimulating Hormone; V – Assessment of Vibratory Sensation with the Tuning Fork; VSA–3000 – Vibration Sensory Analyzer.

Discussion

This review identified 23 distinct diagnostic methods across the 17 included studies, with a greater emphasis on tests aimed at assessing large fibers, followed by those evaluating both large and small fibers, and finally those analyzing small fibers only. A predominance of studies conducted in Asia was observed, followed by Europe and North America. In Brazil, a scarcity of investigations focused on the early detection of diabetic neuropathy (DN) stands out, as most studies are concentrated on diabetic foot, an advanced stage of neuropathic and vascular impairment associated with type 2 diabetes (T2DM).

The progression of DN is closely linked to the loss of protective foot sensation (PPS), a sensory and neural dysfunction that prevents the identification of tactile, pressure, and thermal stimuli. This condition favors mechanical trauma, ulcerations (diabetic foot ulcer – DFU), and, in extreme cases, amputations. Methods such as the 10g monofilament (MF10g) and the Ipswich Touch Test (IpTT) are used to assess PPS; however, both detect DN only in its advanced stages, compromising early detection effectiveness[18].

10g Monofilament

MF10g is considered the gold standard in clinical practice for screening DN, neuropathic pain, and the risk of lower limb ulceration. The test consists of applying the filament to specific points on the soles of the feet with enough force to bend it for 2 seconds. A normal result is the perception of the applied stimulus[19]. When associated with neurological tests (toothpick, 128Hz tuning fork, Achilles tendon reflex hammer, and Tip Therm), it becomes possible to evaluate the loss of plantar protective sensation (PPS). PPS is considered absent when there are at least two incorrect responses in three applications at the same site[1–2].

In the United States, a comparative study showed that the 1g monofilament had higher sensitivity (66.7%) for early detection of DN than the 10g monofilament (47.4%) in overweight adults, using sural nerve amplitude and conduction velocity as a reference. The Norfolk QOL-DN questionnaire had the second-highest sensitivity for early detection[20].

In Austria, comparisons between the MF10g, the Pressure Specified Sensory Device (PSSD), and nerve conduction studies (NCS) showed low correlation and specificity for MF10g, whereas the PSSD showed superior diagnostic performance, including in early stages[21].

Another study indicated that the ankle reflex is the most sensitive sign (64.7%) and absence of vibratory sensation the most specific (93.7%). The MF10g showed the lowest sensitivity (41.1%) and is not recommended as a stand-alone method but rather in combination with other tests such as the 128Hz tuning fork[12].

In China, among 3,883 patients with T2DM, the most sensitive tests were ankle reflex (AR – 50.6%), vibratory sensation (V – 26.6%), and thermal

sensation (T – 24.5%). The most specific test was pinprick (PP – 94.4%). The combinations of AR+T+V or AR+PP+T+V+P were considered the most effective and comparable to NCS[22]. These findings reinforce that using combined methods increases diagnostic accuracy, especially when compared to isolated use of MF10g or other conventional tools[23].

Despite its widespread use, MF10g's limitation in identifying early-stage DN poses both national and international challenges. The Brazilian Diabetes Society recommends caution in its application, given its low sensitivity, considering it more suitable for screening the risk of foot ulceration[16].

Ipswich Touch Test (IpTT)

The IpTT involves lightly touching the first, third, and fifth toes of both feet for 1 to 2 seconds while the patient's eyes are closed. Sensory loss is identified when two or more sites are not felt[24]. In the UK, in a sample of 331 patients with diabetes, the IpTT showed a sensitivity of 76% and specificity of 90%, with strong agreement between home-based and clinical testing. It is easy to perform, well accepted by patients and family members, and can be used as an educational and self-care strategy[25–26].

The Brazilian Diabetes Society recommends the use of tests that assess both small and large fibers, including tactile, thermal, painful, and vibratory sensations[1–6].

Vibration Assessment

Vibratory perception was analyzed using various instruments, such as the 128Hz tuning fork, VibraTip, ETF, and VSA-3000.

The Electronic Tuning Fork (ETF) is a portable and more precise device than the conventional tuning fork, offering timed results. A study in Mexico showed that ETF detected 71 altered sites not identified by conventional methods. It presented a sensitivity of 95.3% and specificity of 76.1%, although the prototype still requires improvements[28].

The VibraTip is a pocket-sized device that simulates 128Hz vibration. In a comparative study in the UK, it identified the highest absence of vibration (28.5%), followed by the neurothesiometer (21%) and the tuning fork (12%). The study recommended using at least two different instruments to assess DN to avoid false negatives and reduce the clinical and economic consequences of late diagnosis[17].

VSA-3000

The VSA-3000 is an automated vibratory sensory analyzer composed of hand and foot stimulators, operating software, and accessories. The test takes 5 to 10 minutes, offers randomized and sham stimulus options, and generates graphs and electronically interpreted data. Results are expressed in micrometers (μm)[30]. A study conducted in Rio de Janeiro evaluated neuropathy using the NDS and NSS scores, the 10g monofilament (MF10g), and the vibratory perception threshold (VPT) assessed by the VSA-3000. The sample was divided into two groups: G1 = ND+ and G2 = ND–. Among the 168

patients with ND+, 39.9% showed abnormalities with the monofilament, and the mean VPT was 16.1 µm. In contrast, among the 66 ND– individuals, only 7% had abnormal MF10g results, and the VPT was 7.4 µm. The VPT progressively increased with the severity of neuropathic signs, with values >8.9 µm associated with a threefold higher likelihood of ND. The sensitivity of the VSA-3000 was 74.4% and its specificity was 57.3%[30].

The following screening methods can be classified as quantitative sensory tests (QST), as they assess sensory thresholds through two or more perceptions (tactile, thermal, painful, or vibratory) combined.

NerveCheck

NerveCheck is a portable device consisting of a remote control unit and a temperature and vibration stimulator. This test can assess thermal perception (hot and cold), vibration, and pain, quantifying the function of large and small sensory fibers. Interpretation depends on the score assigned to each test—the higher the score, the more sensitive the participant is to the stimuli, indicating absence of neuropathy[31]. A study conducted in the United Kingdom evaluated the diagnostic performance of NerveCheck in 144 participants, 74 of whom had DM. These were stratified into G1 = 33 ND+ and G2 = 41 ND– using the Neuropathy Disability Score (NDS). Among the tests performed with NerveCheck, 44 participants had abnormal results: of those with numbness, 65.0% had sensory deficits, whereas 43.0% of those without numbness still showed dysfunction. Among participants with pain complaints, sensory changes were present in 78.0%, while 50.0% of patients without pain had altered responses. Thus, NerveCheck was shown to identify significantly more sensory deficits in people with foot numbness or neuropathic pain compared to those without symptoms, although it provides simple categorical results to identify ND severity[11].

Diabetic Neuropathy Symptom Score (DNS) and Diabetic Neuropathy Examination (DNE)

The Diabetic Neuropathy Symptom Score (DNS) is adapted from the Neuropathy Disability Score (NDS), with a range from 0 to 4 points; a score ≥1 indicates ND. The Diabetic Neuropathy Examination (DNE) consists of eight assessments testing muscle strength, tendon reflexes, and five sensory modalities. The score ranges from 0 to 16, with >3 points considered abnormal[32]. A study in Pakistan compared the effectiveness of the DNS and DNE with nerve conduction studies (NCS). Among 110 volunteers with T2DM, 35 were symptomatic according to the DNS, 38 had abnormal NCS results, and in 8 individuals, both scores were positive. About 30.0% of the sample was asymptomatic but had altered NCS, indicating subclinical ND. It was observed that a positive DNS was not always associated with abnormal NCS, as only 17 out of 35 symptomatic participants had altered conduction. In contrast, 18 patients had a positive DNE, of whom 12 also had abnormal NCS. In this study, the DNS showed a sensitivity of 44.0% and specificity of 73.0%, while the DNE had 31.0% sensitivity and 93.0% specificity. However, when used together, specificity increased significantly to 96.0%[33].

This review highlights Neuropad and Sudoscan as the most effective tests for assessing sudomotor function and, consequently, for the early

detection of ND, as they identify dysfunctions primarily developed in small fibers.

Neuropad

Neuropad is a screening test for ND that visually assesses autonomic sweat dysfunction. It involves the application of a cobalt(II)-based adhesive patch that changes color in response to skin moisture produced by sweat glands. Normal sweat function is identified when the patch changes from blue to pink, indicating preserved autonomic nerve function. However, if the color does not change or the patch does not turn completely pink, it indicates abnormal sweating and, consequently, a higher risk of neuropathic impairment[34].

Neuropad was tested in 1,010 participants with T2DM, divided into G1 = 441 with dysfunction and G2 = 569 without. The method's discriminatory power was interpreted based on two parameters: irregular response (blue and pink color) and abnormal result (blue only). There was a significant correlation between the NDS and Neuropad, with sensitivity over 85.0% and specificity of 71.0% for those with an abnormal result. However, the irregular result is broader and therefore more suitable for screening purposes, as it suggests generalized autonomic and/or small fiber dysfunction. Given its simplicity, objective interpretation, and good discriminatory ability, Neuropad is a useful screening method for identifying early neuropathic dysfunctions, as autonomic changes precede the loss of sensitivity assessed by other methods. Tools such as Neuropad and DPN-Check are not yet available in Brazil's public health system (SUS) but may be implemented in the future due to their high accuracy[35].

Sudoscan

Sudoscan is a non-invasive, automated tool that evaluates sweat gland function. The device includes a computer and four electrodes on which the patient places their bare hands and feet. A low-voltage current (<4 volts) attracts sodium chloride ions from the sweat, reflecting glandular secretion capacity in response to the electrical stimulus. Results are reported as electrochemical skin conductance (ESC) in microsiemens (µS)[36].

In a study with 144 volunteers, tests combining the Michigan Neuropathy Screening Instrument (MNSI) and Sudoscan achieved a higher screening rate (71.7%) compared to the MNSI alone (63.8%). However, pairing MNSI with the 10g monofilament did not significantly improve diagnostic discrimination (67.4%), confirming its insensitivity for early ND detection[13].

Another study in Mexico with 221 participants showed that Sudoscan had superior performance in early ND detection compared to MNSI, which identified abnormalities in 38.4% of the sample, while altered electrochemical conductance was observed in 74.6%[37].

In three other analyses, Sudoscan was compared with nerve conduction studies (NCS), the gold standard for ND diagnosis. Patients with ND+ had lower ESC values and higher foot asymmetry ratios. In another study with 180 participants, 120 had no neuropathy but had a foot ESC of 67 µS, whereas those with ND+ had 53.2 µS[38]. Additionally, an ESC <60 µS was associated with a fivefold increased risk of developing neuropathy. One of the main inconsistencies across studies relates to the cutoff point of foot ESC to detect ND+, which varies between 54 and 60 µS.[15-16,38]

The Sudoscan results were compared to the Neuropathy Symptom Score (NSS) and Neuropathy Disability Score (NDS) in 347 patients, whose sample was divided into three groups: G1 = ND–, G2 = asymptomatic ND+, and G3 = symptomatic ND+. The subgroup showing the greatest abnormalities detected by Sudoscan was G2; however, it was observed that higher scores on the scales were seen in patients with lower ESC values.[14] In another analysis conducted in Mexico, 2,243 participants with a diagnosis of T2DM for less than five years were assessed using Sudoscan, and 27.6% presented with sudomotor dysfunction. In contrast, 29.0% of the sample had neuropathy identified by conventional methods (128Hz tuning fork or 10g monofilament). Although Sudoscan did not detect a higher proportion of individuals with neuropathy, it was concluded that the tests assess different nerve fibers and, consequently, different stages of diabetic neuropathy. Nevertheless, Sudoscan identified a significant number of individuals in the early stage.[15]

It is important to note that the diagnosis of diabetic neuropathy necessarily involves clinical evaluation, foot examination, and exclusion of other neuropathic etiologies. For this purpose, combined screening is essential, including at minimum the ankle reflex test, thermal sensation, and vibratory perception to ensure good diagnostic accuracy.[39–41] In this regard, sensory perception is commonly assessed through subjective methods that rely on the interpretation of both the patient and the examiner. Thus, the use of objective tools may enhance and standardize the screening of diabetic neuropathy. However, such tools require the acquisition of equipment and specialized training.[39]

Furthermore, especially within the Primary Health Care (PHC) setting — the level of care that frequently monitors and manages patients with chronic noncommunicable diseases (NCDs) — the interdisciplinary team and nursing staff must provide holistic, patient-centered, and coherent care strategies. These include health education, promotion of self-care, and preventive actions aimed at delaying complications and improving patients' quality of life.[42–44] Therefore, this represents a moment of professional autonomy and protagonism, especially for nurses, who must be empowered with knowledge about diseases, treatments, and nursing interventions. Nurses are the professionals who maintain the closest contact and interaction with users of the Unified Health System (SUS).

Conclusion

There is a clear need for more research related to early detection of diabetic neuropathy in Brazil, as most existing studies predominantly focus on diabetic foot. This review identified the 10g monofilament (MF10g) as the most widely used screening method in clinical practice, present in 52.9% of the studies analyzed, followed by Sudoscan, present in 35.2% of the sample. However, detection of diabetic neuropathy using the MF10g occurs only at advanced stages, limiting early diagnosis. Therefore, combined screening is essential to maintain good and comprehensive diagnostic accuracy. Tools such as Neuropad, Sudoscan, NerveCheck, and DPNCheck are promising for future

adoption by the Brazilian Unified Health System (SUS), as they are capable of early identification of neuropathy and provide objective, easy-to-interpret data. These instruments may be valuable assets for the multidisciplinary team in the detection and improved survival of individuals with T2DM.

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LIST OF ABBREVIATIONS AND ACRONYMS

ADA – American Diabetes Association
APS – Primary Health Care BDENF – Nursing Database
BVS – Virtual Health Library
DCNT – Non-communicable Chronic Diseases
DeCS – Health Sciences Descriptors
DM – Diabetes Mellitus
DM1 – Type 1 Diabetes Mellitus
DM2 – Type 2 Diabetes Mellitus
DNE – Diabetic Neuropathy Examination
DNS – Diabetic Neuropathy Symptom
ESC – Electrochemical Skin Conductance
ETF – Electronic Tuning Fork
FC – Heart RateHbA1c – Glycated Hemoglobin
IDF – International Diabetes Federation
IpTT – Ipswich Touch Test
LILACS – Latin American and Caribbean Literature in Health Sciences
MEDLINE – Medical Literature Analysis and Retrieval System Online
MeSH – *Medical Subject Headings*
MF – Monofilament
MF10g – 10g Monofilament
MMII – Lower Limbs
MNSI – Michigan Neuropathy Screening Instrument
NCS – Nerve Conduction Study
ND – Diabetic Neuropathy
ND+ – Presence of Diabetic Neuropathy
ND- – Absence of Diabetic Neuropathy
NDS – Neuropathy Disability Score
NPDD – Painful Diabetic Peripheral Neuropathy
NSS – Neuropathy Symptom Score
PAD – Diastolic Blood Pressure
PEP – Loss of Protective Sensation in Feet
PSSD – Pressure Specified Sensory Device
PubMed – U.S. National Library of Medicine National Institute of Health
QOL-DN – Norfolk Quality of Life-Diabetic Neuropathy
QST – Quantitative Sensory Testing
RI – Integrative Literature Review
SBD – Brazilian Society of Diabetes
SNAP – Sural Nerve Action Potential
SNCV – Sural Nerve Conduction Velocity
SUS – Unified Health System
UPD – Diabetic Foot Ulcer
VPT – Vibratory Perception Threshold
VSA–3000 – Vibration Sensory Analyzer

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