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Detection of undisclosed neuropathy and assessment of its impact on quality of life: a survey in 25,000 Romanian patients with diabetes

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ABSTRACT

Aims: The objective of this cross-sectional survey was to capture undiagnosed neuropathy in Romanian patients with self-reported diabetes using Norfolk QoL-DN as a screening tool and to assess its impact on quality of life (QoL).
Methods: 25,000 Romanian-translated, validated Norfolk QoL-DN questionnaires were distributed between June and December 2012. 21,261 patients who self-reported diabetes and answered questions related to neuropathy, ulceration, gangrene and amputation were included in the analysis.
Results: 52% of diabetic patients (n = 6615) who answered "no" to the question "Do you have neuropathy?" had total QoL scores above the cut-off, suggesting the presence of diabetic neuropathy. 13,854 (65.2%) patients answered "yes" to the question "Do you have neuropathy?" and 3,150 (14.8%) reported at least one episode of ulceration, gangrene or amputation. Total QoL score was 3-fold higher (worse) for patients who answered "yes" to the question "Do you have neuropathy?" than for those who answered "no" (38.39 vs. 13.71; $p < 0.001$) and 1.4-fold worse for patients who reported ulceration, gangrene or amputation than for those who did not report any of these (50.38 vs. 34.87; $p < 0.001$).
Conclusions: We found a high prevalence of undisclosed diabetic neuropathy in this population and showed that neuropathy severity has an increasing impact on total QoL and its domains.

1. Introduction

The International Diabetes Federation (IDF) published a report in 2013 of an estimated 385 million people with diabetes worldwide, the majority being diagnosed with type 2 diabetes; the epidemiologic projections for the year 2035 now estimate an increase to 592 million (International Diabetes Federation, 2013).

In Romania, 482,250 patients were registered as beneficiaries of the National Program for Diabetes in 2005 (Ministerul Sanatatii, 2011). This figure increased in 2011 to 803,489 with a prevalence of 4.21% in the country (Mota & Dinu, 2013). The IDF estimated that the prevalence of diabetes in Romania had increased to 5.1% in 2013 and will reach 6.4% in 2035 (International Diabetes Federation, 2013).

The social, economic and medical burden of diabetes represents an enormous public health problem, raising diabetes to the 4th cause of death worldwide (International Diabetes Federation, 2009). Moreover, the devastating micro- and macrovascular complications associated with diabetes significantly reduce quality of life (QoL) and life expectancy (International Diabetes Federation, 2009; Koopmanschap & Board, 2002).

Diabetic neuropathy, one of the most common chronic complication (Vinik, Nevoret, Casellini, & Parson, 2013), is associated with substantial morbidity and an increased risk of recurrent foot infections and ulcerations, accounting for 50–75% of non-traumatic lower limb amputations (Little, Edwards, & Feldman, 2007; Vinik

Conflict of interest: Etta J. Vinik and Aaron I. Vinik have a patent copyright of the Norfolk QOL-DN. Eastern Virginia Medical School engaged in a licensing agreement with Wörwag; royalties were paid to Etta J. Vinik and Aaron I. Vinik. Cosmina I. Bondor reports non-financial support from Wörwag Pharma GmbH&Co.KG, Romanian Rep Office during the conduct of the study. Andrei I. Veresiu reports personal fees (speaker fees) from Wörwag Pharma GmbH&Co.KG, Romanian Rep Office, outside the submitted work. Norina A. Gâvan is an employee of Wörwag Pharma GmbH&Co.KG, Romanian Rep Office. Bogdan Florea has nothing to disclose.

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et al., 2013). Due to inconsistent definitions used in epidemiological trials, the reported prevalence of diabetic neuropathy varies widely, from 23% to 70% (Dyck et al., 1993; Pop-Busui, Lu, Lopes, Jones, & BARI 2D Investigators, 2009; Tesfaye et al., 1996; Young, Boulton, MacLeod, Williams, & Sonksen, 1993; Young, Every, & Boulton, 1993). In Romania, the data on the prevalence of diabetic neuropathy have been scarce (Cegedim, 2014; Cobuz & Cobuz, 2012; Tesfaye et al., 1996). The most recent data come from a survey organized in 2013 by a market research company from interviews with Romanian physicians, specialists in diabetes, who reported a prevalence of diabetic neuropathy of 44% (Cegedim, 2014).

The Norfolk Quality of Life Questionnaire-Diabetic Neuropathy (Norfolk QoL-DN) is a nerve fiber-specific validated assessment tool, specific to diabetic neuropathy, comprising five factors or domains representing separate neuropathic disabilities attributed to different nerve fibers. The total QoL score has been previously shown to correlate with the total objective neuropathy score (Vinik, Stansberry, & Vinik, 2003; Vinik et al., 2000; Vinik et al., 2005). Importantly, Norfolk QoL-DN has been shown to have good sensitivity (78.95%), specificity (85.03%), positive (86.57%) and negative (76.77%) predictive values (using as reference the San Antonio Consensus criteria for neuropathy) (Consensus statement, 1988), strongly suggesting its use as a screening tool for diabetic neuropathy (Vinik et al., 2000).

Previously published data on the impact of diabetic neuropathy on QoL comes from relatively small studies (Solli, Stavem, & Kristiansen, 2010; Vinik, Paulson, Ford-Molvik, & Vinik, 2008; Vinik & Vinik, 2007), and no data are available for Romania. To address the impact of diabetic neuropathy and its severity on the QoL of Romanian patients with self-reported diabetes, we designed a survey using the Norfolk QoL-DN as a screening tool. Our main objectives were to screen a large population of patients with self-reported diabetes for undetected diabetic neuropathy and to evaluate the impact of self-reported neuropathy on QoL.

2. Subjects, materials and methods

2.1. Protocol and study population

In this cross-sectional survey, conducted between June and December 2012, 181 healthcare providers (153 physicians diabetes specialists, 5 neurologists, 14 general practitioners and 9 nurses — also diabetes specialists) from 51 Romanian cities distributed the linguistically translated Romanian Norfolk QoL-DN questionnaire to patients with diabetes from their clinics. The Norfolk QoL-DN was self-completed by all outpatients who agreed to participate. Patients were informed that their personal data would be analyzed anonymously as part of a survey registered with the Romanian authorities. All patients who participated consented for their data to be included in the analysis. No information on the type of diabetes was collected.

The data collection was approved by The National Supervisory Authority for Personal Data Processing and was supervised by the Epidemiology Department of the Iuliu Ha ieganu University of Medicine and Pharmacy of Cluj-Napoca.

2.2. The Norfolk Quality of Life diabetic neuropathy questionnaire

The Romanian version was professionally linguistically translated by Oxford Outcomes, Oxford, UK from the original USA English version, using a strict methodology with quality control checks that included two independent forward translations of the original, a reconciliation of the two forward translations, a backward translation (conceptually validated by experts at Eastern Virginia Medical School, Norfolk, VA, US) and finally a cognitive debriefing by testing the new language tool on at least 5 patients with diabetic neuropathy. The Norfolk QoL-DN has been validated across the spectrum of neuropathy severity (Vinik et al., 2008) and translated into 47 different languages for clinical trials.

The Romanian translation of the Norfolk QoL-DN, like the original version, is a self-administered questionnaire comprising items related to patients' signs, symptoms, and the impact of diabetic neuropathy on their daily life. Items on the first page capture demographic and medical history data and include “yes” or “no” responses to the following questions: “Do you have diabetes?” “Do you have neuropathy?” “Have you ever had ulcers on your feet”, “Have you ever had gangrene” and “Have you ever had any amputations?” Most of the 35 QoL items on the questionnaire are scored on a 5-point Likert scale ranging from 0 (“no problem”) to 4 (“severe problem”), and patients are asked to refer to the past 4 weeks when answering these questions. Higher scores reflect a poorer QoL. In items 1 — 7 of the scored questionnaire, patients are asked to select the type of neuropathy symptoms from a vertical list and to identify their localization (listed horizontally as feet, legs, hands, and arms) with a check mark. Items 8–35 are related to patients' responses to queries on activities of daily life; most of the items are scored.

The range of possible scores for the Norfolk QoL-DN domains are: —4 — 136 for total QoL score; —4 — 56 for physical functioning/large-fiber neuropathy, 0 — 32 for symptoms, 0 — 20 for the activities of daily living, 0 — 12 for autonomic neuropathy and 0 — 16 for small-fiber neuropathy. The negative values arise from the fact that questions 31 and 32 are scored differently and can have negative scores. Using the mean and 2 standard deviations of the range of possible scores we calculated the cut-off values for the Norfolk QoL-DN domains: 5 for total QoL score; 0.5 for physical functioning/large-fiber neuropathy, 1 for symptoms, 4 for the activities of daily living, 1 for autonomic neuropathy and 1 for small-fiber neuropathy. The cut-off values were obtained in patients with established neuropathy during the validation of QoL-DN in a patient population with mild neuropathy (Vinik et al., 2005) based on the San Antonio criteria (Consensus statement, 1988). We considered the scores higher than these cut-off values as suggestive for the presence of neuropathy (Vinik et al., 2008).

The normative data for the total QoL score and the five sub-domains (Vinik et al., 2005), previously calculated in persons without diabetes, are: 3.8 for total QoL score, 0.3 for physical functioning/large-fiber neuropathy, 0.7 for symptoms, 3.1 for the activities of daily living, 0.5 for autonomic neuropathy and 0.6 for small-fiber neuropathy.

Differences in the total and subdomain QoL scores between different groups >10% of the maximum value for the total score and for each specified subdomain scores were considered to be clinically significant — i.e. 13.6 for total score, 5.6 for physical functioning/large-fiber neuropathy; 3.2 for symptoms; 2.0 for the activities of daily living; 1.2 for autonomic neuropathy; and 1.6 for small-fiber neuropathy. Cut-off values for clinical significance have been derived from the means and 2 standard deviations of the total QoL score and each of its domains representing “normality”. Scores greater than the cut-offs suggest neuropathy (please see Table 1 for cut-offs).

2.3. Analysis of data

To ensure anonymity, all patient identification data were removed, and the data from the questionnaires were entered into to a Microsoft Excel worksheet by a team of six IT specialists.

A questionnaire was considered valid and was included in the analysis if complete biographic information was provided including age and sex. However, only the questionnaires from those who answered “yes” to the question, “Do you have diabetes?” were included in the analysis. Additionally, the diabetes group was divided into those with and without self-reported neuropathy according to their “yes” or “no” answers to the question “Do you have neuropathy?” The questionnaires without answers to the question “Do you have