European Journal of Cancer 69 (2016) 28–38

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

Original Research

Reference data of the European Organisation for Research and Treatment of Cancer (EORTC) QLQ-CIPN20 Questionnaire in the general Dutch population

Floortje Mols [a,b,*], Lonneke V. van de Poll-Franse [a,b,e], Gerard Vreugdenhil [c,d], Antoinetta J. Beijers [c], Jacobien M. Kieffer [e], Neil K. Aaronson [e,f], Olga Husson [g]

[a] *Department of Medical and Clinical Psychology, Tilburg University, Tilburg, The Netherlands*
[b] *Department of Research, Netherlands Comprehensive Cancer Organisation (IKNL), Utrecht, The Netherlands*
[c] *Department of Internal Medicine, Máxima Medical Centre, Eindhoven and Veldhoven, The Netherlands*
[d] *Department of Medical Oncology, GROW – School for Oncology and Developmental Biology, Maastricht University Medical Centre, Maastricht, The Netherlands*
[e] *Department of Psychosocial Research, Division of Psychosocial Research and Epidemiology, The Netherlands Cancer Institute, The Netherlands*
[f] *Department of Clinical Psychology, The University of Amsterdam, The Netherlands*
[g] *Department of Medical Psychology, Radboud University Medical Center, Nijmegen, The Netherlands*

Received 19 April 2016; received in revised form 1 September 2016; accepted 13 September 2016
Available online 1 November 2016

KEYWORDS
Chemotherapy-induced peripheral neuropathy;
EORTC QLQ-CIPN20;
Normative data

Abstract ***Objective:*** Chemotherapy-induced peripheral neuropathy (CIPN) is a debilitating side-effect of chemotherapy. However, CIPN symptoms are also reported by patients not receiving chemotherapy. Normative data could help interpret CIPN among cancer patients. Our aim was to generate normative data for the European Organisation for Research and Treatment of Cancer (EORTC) QLQ-CIPN20 Questionnaire designed to assess CIPN from the patients' perspective. The normative CIPN data have also been generated for stratified subgroups formed on the basis of sex, age and comorbidity.
Methods: The QLQ-CIPN20 and the Self-administered Comorbidity Questionnaire were administered to a representative panel of the Dutch-speaking population in the Netherlands.
Results: Two thousand one hundred and two (78%) of those invited completed the questionnaires. The majority reported no CIPN symptoms (83–97%). Cronbach's alpha coefficients for the sum score, and sensory, motor and autonomic subscales were 0.87, 0.76, 0.82 and 0.49, respectively. Compared with men, women scored significantly worse on the sum score (men, 3.0 versus women, 4.3; $p < 0.001$), motor scale (2.7 versus 5.1; $p < 0.001$) and autonomic

* *Corresponding author*: Department of Medical and Clinical Psychology, Tilburg University, PO Box 90153, 5000 LE Tilburg, The Netherlands.
E-mail address: F.Mols@tilburguniversity.edu (F. Mols).

http://dx.doi.org/10.1016/j.ejca.2016.09.020

scale (3.8 versus 5.2; $p < 0.01$), but this difference was not clinically relevant. CIPN symptoms increased significantly with age among both men (for the sum score and all scales) and women (for the sum score, sensory and motor scale). Those with self-reported comorbidities reported significantly more CIPN symptoms, both statistically and clinically, than those without. For instance, they had a lower mean sum score (1.5) compared to those with asthma/chronic obstructive pulmonary disease (COPD; 6.9), diabetes (5.9), heart disease (8.0), hypertension (6.2), osteoarthritis (9.6) and rheumatoid arthritis (13.8).

Conclusions: A low prevalence of neuropathy was observed in the normative population without cancer, although neuropathy did increase with age and the presence of comorbidities. These data (which is freely available) can aid in the interpretation of QLQ-CIPN20 scores and can help increase our understanding of the influence of age, sex and comorbid conditions on CIPN among cancer patients.

1. Introduction

Chemotherapy-induced peripheral neuropathy (CIPN) is a debilitating side-effect of chemotherapy. Usually, CIPN begins with sensations of burning, numbness, tingling, itching or prickling and an abnormal, unpleasant sense of touch in the toes and fingers that can spread to the arms and legs [1]. CIPN can occur due to treatment with chemotherapeutic agents like taxanes, platinum derivatives, vinca alkaloids, thalidomide and bortezomib [2–5]. The severity of CIPN symptoms depends mainly on the type of chemotherapy used, cumulative dose, duration of administration and pre-existing neuropathy [5,6].

Since the prevalence of cancer is rising [7], and current indication of chemotherapy use is expanded with new chemotherapeutic agents with CIPN side-effects [8], the prevalence of CIPN is also on the rise.

CIPN is often only partly reversible and sometimes irreversible [4,5,9]. Despite many efforts, there are currently no effective preventive strategies or treatments available for CIPN [10]. Lowering the dosage of chemotherapy promptly after serious CIPN symptoms occur is currently the only way of reducing the risk for CIPN. This, however, may result in reduced chemotherapy efficacy. Therefore, it is important to monitor CIPN in a valid and reliable manner during treatment. As clinical tests to assess CIPN are not always patient friendly, not truly objective, time-consuming, expensive and often not sensitive enough to detect beginning CIPN, the addition of patient-reported outcomes measures to clinical tests is preferred [10–12].

There are many patient-reported outcomes available that assess CIPN, but a gold standard has yet to be determined. However, the American Society of Clinical Oncology (ASCO) guideline on the prevention and management of CIPN recommends some measures, of which the European Organisation for Research and Treatment of Cancer (EORTC) QLQ-CIPN20 is one [10,13]. This questionnaire was developed by the EORTC to assess patients' experience of symptoms and functional limitations related to CIPN. The questionnaire can be scored in a number of ways, including the use of three subscales based on type of CIPN (i.e. sensory, motor and autonomic) [13,14] and of a sum score [15].

The use of the EORTC QLQ-CIPN20 subscale scores for individuals in daily clinical practice, with the purpose of deciding on the necessity of dose modifications, is difficult since existing guidelines on dose modifications are based on the National Cancer Institute-Common Toxicity Criteria for Adverse Events (NCI-CTCAE) [16]. As a result, the EORTC QLQ-CIPN20 is more often used in cancer research than in clinical practice. CIPN symptoms can also be present among those not (yet) treated with chemotherapy, but data on this matter are scarce [17]. The EORTC QLQ-CIPN20 has proven to be a valuable research tool. Researchers often try to interpret its scores by making comparisons between those treated with different forms or doses of chemotherapy, or by comparing those treated with or without chemotherapy. The interpretation of the EORTC QLQ-CIPN20 scores could be improved if one would also be able to compare CIPN scores of a particular study with age- and gender-matched normative data from the general population without cancer, to see the true effect of both cancer and its treatment on CIPN. These normative data also allow researchers to estimate whether differences are clinically meaningful [18].

Normative data on self-reported peripheral neuropathy using the QLQ-CIPN20 has, to our knowledge, not been reported previously in the literature. The aim of the present study was therefore to generate Dutch normative data for the QLQ-CIPN20, including results stratified by sex, age and comorbid conditions. Also, normative data for those ever diagnosed with cancer were collected.

2. Materials and methods

2.1. Setting and study population

Normative data were obtained by adding the QLQ-CIPN20 Questionnaire to the 2014 wave of the Health