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Course of chemotherapy-induced peripheral neuropathy and its impact on health-related quality of life among ovarian cancer patients: A longitudinal study

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HIGHLIGHTS

- Sensory neuropathy symptoms were stable over time.
- Motor neuropathy symptoms improved at 1 year.
- A high level of sensory neuropathy was associated with worse functioning.
- A high motor neuropathy level was associated with worse HRQoL.

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ABSTRACT

Objective. Chemotherapy-induced peripheral neuropathy (CIPN) presents itself as sensory peripheral neuropathy (SPN) or motor peripheral neuropathy (MPN). Our aim was to examine the course of SPN and MPN, and their impact on health-related quality of life (HRQoL) among ovarian cancer patients.

Methods. All newly diagnosed ovarian cancer patients from twelve hospitals in the South of the Netherlands were eligible for participation. Patients (N = 174) completed questions on CIPN (EORTC QLQ-OV28) and HRQoL (EORTC QLQ-C30) after initial treatment and at 6, 12, and 24 months (response rates were 70%, 71%, 58%, and 43% respectively).

Results. Generalized linear mixed models showed that among chemotherapy-treated patients (N = 98), SPN levels were stable over time. For MPN, symptoms significantly improved at 12 months. At 2 years, 13% still reported high SPN. Also, 11% still reported high MPN. Regarding HRQoL, patients with high SPN reported a worse physical, role, emotional, social, and cognitive functioning compared to those with low SPN. Moreover, those who changed from low to high SPN over time worsened on physical functioning. For MPN, a worse global quality of life and a worse functioning was reported among patients with high MPN. Also, those who changed from low to high MPN over time worsened on global quality of life and on physical, role, social, and cognitive functioning.

Conclusions. Among chemotherapy-treated ovarian cancer patients, SPN levels were stable over time. In contrast, MPN symptoms significantly improved at 12 months. These symptoms seriously impacted HRQoL. Future studies should examine the impact of different treatment decisions and alterations on CIPN, so recommendations can be made to reduce CIPN (prevalence).

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1. Introduction

Ovarian cancer was one of the first solid tumors for which effective chemotherapy became available with the introduction of cisplatin in 1978. The addition of paclitaxel to the standard chemotherapy regime in 1994 improved survival rates [1–3]. Unfortunately, chemotherapy-induced peripheral neuropathy (CIPN), one of the most life-affecting side effects of chemotherapy, has become a major concern. CIPN interferes with optimal cancer treatment, as it is often needed to reduce chemotherapy doses and delay treatment and it may even lead to premature cessation of treatment. Unfortunately, there is currently no well-accepted treatment or prevention strategy against CIPN [4].

CIPN can present as sensory peripheral neuropathy (SPN) (i.e. numbness, tingling, cramps and pain in the fingers, hands, toes, and feet) and motor peripheral neuropathy (MPN) (i.e. weakness, muscle wasting, cramps or fasciculation) [5]. These symptoms can cause problems with regular daily activities, such as buttoning a shirt or opening a bottle, but also with walking or driving [6,7].

While symptoms of CIPN often reverse or improve in the first few months after treatment, a significant proportion of cancer patients experience chronic CIPN. Also, CIPN symptoms can develop years after completion of chemotherapy treatment [8–11].

Given the serious limitations in daily functioning that accompany CIPN, it could also have a negative impact on health-related quality of life (HRQoL) [8,11–14]. In ovarian cancer, three cross-sectional studies and one longitudinal study have examined the relationship between CIPN and HRQoL, with mixed findings [11,13,15,16]. Also, no longitudinal study has examined the course of CIPN over time and its impact on HRQoL after treatment has ended.

Understanding the impact of CIPN can help inform both clinicians and patients about the possible side effects of cancer treatment. As the symptoms of SPN and MPN are distinctly different from one other, they could have a different course as well as different effects on HRQoL. Therefore, this study aims to prospectively assess the course of SPN and MPN and their relationship with HRQoL among ovarian cancer patients up to 2 years after diagnosis. We hypothesize that both SPN and MPN will show either a stable course or a small decline after 6 months among chemotherapy-treated patients, while we expect both courses to be stable among those treated without chemotherapy. Furthermore, we expect that both SPN and MPN will be related to a worse HRQoL.

2. Methods

2.1. Setting and participants

This study is a secondary analysis of the ROGY Care trial; a longitudinal, pragmatic cluster-randomized trial among patients with gynecological cancer, aimed to gain insight in the effect of an automatically generated Survivorship Care Plan (SCP) on patient- and health care provider-reported outcomes [17]. Twelve hospitals in the South of the Netherlands were randomly assigned to either “usual care” or “SCP care”, in which patients received a SCP. All patients newly diagnosed with ovarian cancer and endometrial cancer as a primary tumor between April 2011 and March 2014 were eligible for participation. Patient exclusion criteria (i.e., borderline ovarian cancer, undergoing palliative care, or unable to complete a Dutch questionnaire) were minimal to maximize generalizability [18]. For this study, we only selected ovarian cancer patients. We included those treated with and without chemotherapy as previous studies have shown that CIPN-like symptoms were already present in those who did not (yet) receive chemotherapy [19,20]. The ROGY Care trial was centrally approved by a Medical Research Ethics Committee, as well as by each participating center.

2.2. Data collection

Shortly after initial treatment, all eligible patients were invited to participate in the study via a letter with informed consent form and the first questionnaire that were send by their own gynecologist [21]. For this analyses we used outcomes assessed at baseline (T1) and at 6 (T2), 12 (T3), and 24 months (T5).

2.3. Sociodemographic and clinical characteristics

Patients' sociodemographic (i.e., age and socioeconomic status) and clinical (e.g., cancer type, FIGO stage, date of diagnosis) data were available from the Netherlands Cancer Registry (NCR), which routinely collects data on newly diagnosed cancer patients in all hospitals in the Netherlands [21]. Other sociodemographic data (e.g., partner status, educational level, and employment status) were assessed with the first questionnaire. Comorbidity was assessed with the adapted Self-administered comorbidity questionnaire (SCQ) [22]. Data on the presence of a recurrence were retrospectively extracted from the medical records two years after completion of inclusion of the trial.

2.4. Health-related quality of life

The EORTC QLQ-C30 (Version 3.0) was used to assess HRQoL. In this study, only the five functioning scales and the global quality of life scale were used. Items are answered on a 4-point Likert scale ranging from

Table 1
Sociodemographic and clinical characteristics at T1 of ovarian cancer patients who completed at least two questionnaires, stratified by chemotherapy.

	Chemotherapy N = 98 (80%)	No chemotherapy N = 25 (20%)	p-Value
Age (mean, SD)	64.8 (9.7)	59.6 (11.8)	**0.02**
Partner (yes)	75 (77%)	16 (67%)	0.32
Educational level[a]			0.23
Low	15 (16%)	1 (4%)	
Medium	61 (63%)	15 (63%)	
High	21 (22%)	8 (33%)	
Socio-economic status			0.82
Low	15 (17%)	5 (22%)	
Medium	33 (38%)	9 (39%)	
High	40 (46%)	9 (39%)	
Employment (yes)	25 (26%)	11 (46%)	0.05
ROGY Condition			0.55
Care as usual	33 (34%)	15 (60%)	
Intervention	65 (66%)	10 (40%)	
FIGO stage at diagnosis			<**0.001**
1	13 (14%)	24 (96%)	
2	12 (13%)	1 (4%)	
3	51 (53%)	–	
4	20 (21%)	–	
Surgical treatment	91 (93%)	25 (100%)	0.34
Number of comorbidities			0.75
None	25 (26%)	5 (21%)	
One	29 (30%)	9 (38%)	
Two or more	43 (44%)	10 (42%)	
Comorbidities associated with PN[b]			
Osteoarthritis	25 (33%)	8 (44%)	0.36
Rheumatoid arthritis	12 (17%)	4 (24%)	0.51
Diabetes mellitus	19 (26%)	5 (28%)	0.99
CIPN (Mean, SD)[c]	40.3 (30.8)	10.2 (16.0)	<**0.001**
Sensory neuropathy (Mean, SD)	41.3 (37.5)	7.6 (17.0)	<**0.001**
Motor neuropathy (Mean, SD)	38.1 (32.4)	15.3 (21.9)	<**0.001**

Variables may deviate from 100% due to rounding off.
SD standard deviation. Bold p-values indicate statistically significance.
[a] Education: low (no or primary school); medium (lower general secondary education or vocational training); high (pre-university education, high vocational training, university).
[b] Most frequent comorbidities associated with chemotherapy-induced peripheral neuropathy.
[c] Total score of the peripheral neuropathy scale of the EORTC QLQ-OV28.

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