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Functional loss in daily activity in ovarian cancer patients undergoing chemotherapy

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Abstract

Purpose Cancer survivors frequently experience cancer or treatment-related symptoms and functional morbidities that can be addressed through rehabilitation services, but these symptoms often go unnoticed and seldom managed. This study seeks to investigate the undetected patient symptoms and functional loss related to the activities of daily living (ADLs) in ovarian cancer patients during chemotherapy and to identify the influence of chemotherapy on such loss.

Methods Ovarian cancer patients undergoing chemotherapy were identified from June to August 2016, who were treated at the department of Gynecology and Obstetrics of two tertiary hospitals. The questionnaires on the present cancer and treatment-related symptoms, patient recognition of rehabilitation needs, and the Katz index score were collected.

Results Records of total 168 ovarian cancer patients were selected and reviewed. The majority of patients (93.5%) experienced at least one symptom, with paresthesia (76.2%), fatigue (63.1%), pain, muscle weakness, memory and concentration dysfunction, lymphedema, breathing discomfort, dysphagia, and speech difficulty being the primary complaints in descending order. About 20% of ovarian cancer patients under chemotherapy had functional dependence in ADLs. The most affected ADL functions were continence, bathing, transfer, and dressing in descending order. Fatigue symptom and the functional dependence showed a significant correlation in proportion to the total number of chemotherapy cycles.

Conclusions There are undetected symptoms and functional loss in ovarian cancer patients during chemotherapy, which aggravated in relation to the increase in accumulated chemotherapy. Timely and appropriate rehabilitative intervention may help minimize these symptoms and functional loss, and further contribute to the improved quality of life.

Keywords Ovarian neoplasm · Chemotherapy · Symptom · Function · Activities of daily living

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Introduction

With the aging of society, there have been improvements in cancer screening, cancer-directed therapies, and management strategies. These medical advances have led to the early detection of cancer and extended life expectancy after initial cancer diagnosis. Due to this prolongation of the cancer care continuum, patient quality of life for this growing group has become an important area of cancer care. This new perspective has shifted the focus of cancer surveillance from a cancer control perspective to a more comprehensive care including provision of rehabilitation services to address and manage long-term consequences of cancer and its treatment [1]. Accordingly, improving the quality of life (QOL) of cancer patients including the function in daily activities during the clinical trajectory after diagnosis has become a new task.

Among the various kinds of cancer, ovarian cancer is the seventh most common cancer in women, with 240,000 women newly diagnosed worldwide every year [2]. The standardized treatment for ovarian cancer is tumor-reductive surgery or appropriate surgical staging followed by chemotherapy [3]. Unfortunately, among the primary ovarian cancer patients under chemotherapy, the majority of women, up to 80%, will eventually experience disease recurrence leading to the continuation of either the same chemotherapy regimen or a switch to second-line agents [3, 4]. This characteristic of ovarian cancer changes the treatment course from that of a acute soon-to-be-fatal condition to that of a chronic disease [3]. Moreover, this chronic illness character of ovarian cancer can deteriorate the quality of life of patients undergoing treatment, which has been observed in ovarian cancer survivors and contributes to the overall survival in this population [5].

There have been several studies assessing and attempting to improve the quality of life of cancer patients [6, 7]. Many have demonstrated the benefits of rehabilitation in improving the quality of life of cancer patients, and although not as well studied, these benefits extend even to patients with advanced-stage cancer [8]. Despite the beneficial effects of rehabilitation in alleviating functional impairments in chronically ill patients, including cancer survivors, rehabilitation services are underused in all phases of cancer care [9, 10]. Moreover, there is still a lack of screening tools and processes for the early detection of such symptoms and functional loss in the patients as an effort to improve their health-related QOL. Objective assessment and timely management of physical health and function are needed to promote improved health-related quality of life of cancer patients under treatment.

Studies regarding ovarian cancer patients under chemotherapy are only a few. Unlike breast cancer, another female cancer where there have been numerous studies of quality of life and functions in patients undergoing active treatment [11, 12], there have only been a few studies on that of ovarian cancer patients undergoing chemotherapy. Moreover, there are no studies on detailed assessment of functional loss in activities of daily living (ADLs) and treatment-related symptoms that are remediable to rehabilitation intervention. Yet, the actual rehabilitation needs of ovarian cancer patients are often underestimated and missed due to reasons such as poor recognition and referral from other departments. Thus, although most cancer survivors experience cancer treatment-related functional morbidities that can be mediated through rehabilitation services, this functional loss often goes unnoticed and is seldom managed due to the lack of comprehensive cancer care and the physicians' focus on progression-free survival of patients, rather than maintenance of function [10].

The aim of this study is to examine the undetected symptoms and functional loss, and their correlation in ovarian cancer patients undergoing chemotherapy and to identify the influence of chemotherapy.

Materials and methods

Subjects

The medical records of inpatient ovarian cancer patients undergoing chemotherapy treated at the department of Gynecology and Obstetrics of two tertiary hospitals from June to August 2016 were reviewed. To exclude the patients with other medical comorbidities that have influence in their physical performance, we excluded the following: (a) patients with severe cancer complications such as ascites, pleural effusion or kidney failure; (b) patients under radiotherapy or with history of radiotherapy; (c) patients with combined additional primary cancer; and (d) patients with cerebrovascular accident, neuromuscular disease, or other diseases that cause motor weakness.

Methods

The general information of patients such as age, marital status, educational status, diabetes, and hypertension was collected. Cancer stage with additional information on recurrence state, chemotherapy regimen, and the total number of chemotherapy cycles was also recorded. The questionnaires on the presence of cancer and cancer treatment-related symptoms, and on the patient's awareness and recognition of the rehabilitation needs were done. The Katz index score from a nursing chart was collected to determine the effect of cancer treatment on daily living activities. All the medical records were based on patient-reported outcomes.

The Katz index is a dichotomous scale used to assess the independence of patients in ADLs. The index includes performance in six functions (bathing, dressing, toileting, transferring, continence, and feeding) with a total score of six points. A score of six indicates full function, 3–5 indicates moderate impairment, and two or less indicates severe functional impairment.

The presence of cancer and cancer treatment-related symptoms related to rehabilitation was collected using the questionnaire form from a similar previous study [13]. The symptoms include pain, paresthesia, muscle weakness, fatigue, memory and concentration dysfunction, lymphedema, dysphagia, speech dysfunction, and breathing difficulty. Each symptom was assessed on a three-point scale, from 0 to 3 in an increasing manner according to severity. Also, the questionnaires about awareness and subjective needs of rehabilitation for each symptom were evaluated.

The study was approved by the Institutional Review Boards of two tertiary hospitals (IRB file no.: SMC2016-10-062 and NCC2016-0289).

Statistical analysis

Mean and standard deviation for continuous variables and proportions for binary variables were used to summarize the subject characteristics. Independent *t* test and Spearman correlation analysis were performed to discriminate the relationship between the number of chemotherapy cycles and the dependence in functional domains of the Katz index. Kruskal–Wallis test was performed to identify the relationship between the groups divided according to the total number of chemotherapy cycles and the severity of the cancer or cancer treatment-related symptoms.

Fatigue symptoms and total Katz score were selected for multiple linear regression analysis to estimate the genuine influence of accumulated chemotherapy on them. All analyzes were performed using SPSS version 23.0, SPSS Inc., Chicago, IL, USA.

Results

Study participants

Total 168 patients meeting the inclusion criteria were enrolled in the study. The general characteristics of the participants are described in Table 1. About half of the participants were stage III, and the remaining were stage IV, II, and I, in decreasing order. There were 118 primary cancer patients, and the rest of the participants were recurrent ovarian cancer patients. The median total number of chemotherapy cycles at the time of the study was 8 (8.06 ± 8.08). Most of the patients (91.1%) had history of surgery either as primary or interval debulking surgery. Out of 15 patients without surgery, 9 patients had surgery scheduled in short future after the study enrollment. The rest of the patients did not have surgery due to reasons such as severe asthma and patient refusal.

Table 1 General characteristics of participants ($N = 168$)

Characteristics	Mean ± SD
Age (years)	54.26 ± 10.54
Marital status, *n* (%)	
Married	139 (82.7%)
Single	9 (5.4%)
Widowed	9 (5.4%)
Divorced	11 (6.5%)
Education status, *n* (%)	
None	1 (0.6%)
Elementary school diploma	19 (11.3%)
Middle school diploma	19 (11.3%)
High school diploma	67 (39.9%)
College diploma	50 (29.7%)
Postgraduate diploma	12 (7.2%)
FIGO stage, *n* (%)	
I	9 (5.4%)
II	21 (12.5%)
III	97 (57.7%)
IV	41 (24.4%)
Chemotherapy cycles	8.06 ± 8.08
Recurrent cancer patient ($n = 50$)	15.1 ± 10.39
Primary cancer patient ($n = 118$)	5.08 ± 4.30
Surgery, *n* (%)	153 (91.1%)

SD standard deviation

Symptoms

The symptoms and their severity scores based on a three-point scale are described in Table 2. Out of 168 patients, 157 (93.5%) had at least one subjective symptom. The most common symptoms were paresthesia (76.2%), fatigue (63.1%), pain, muscle weakness, memory and concentration dysfunction, lymphedema, breathing discomfort, dysphagia, and speech difficulty, in descending order (Fig. 1). Except for paresthesia and fatigue, the severity of other symptoms was mild with less than one point on the three-point scale. As to see the influence of chemotherapy, the relation between symptom severity and the number of chemotherapy cycles was analyzed by grouping the patients according to their total number of cycles done at the time of evaluation. Paresthesia, fatigue, and pain showed a significant correlation to the total number of chemotherapy, with severity of paresthesia and fatigue showing increasing proportional correlation to the total number of cycles.

Among the possible factors that may contribute to the presence of fatigue, including age, marital and education status, the presence of other comorbidities such as diabetes mellitus and hypertension, recurrence, cancer stage (FIGO), and total number of chemotherapy cycles, multivariate regression analysis revealed the number of chemotherapy cycles to be the sole significant factor (Table 4). Table 4 presents the results of linear regression analysis to identify the factors that are associated with fatigue. Recurrence was significantly associated with the severity of fatigue symptom, but it did not meet the criteria in the multivariate model ($p = 0.502$). In contrast, the number of chemotherapy cycles at the data collection point was significantly associated with fatigue in both univariate and multivariate models. In the final multivariate model, when all the other factors were adjusted, a one-cycle

Table 2 Severity of symptoms in ovarian cancer patients during chemotherapy ($N = 168$)

Symptoms	Number, *n* (%)	Total score	Gp 1 ($n = 99$)	Gp 2 ($n = 39$)	Gp 3 ($n = 30$)	*p* value
Paresthesia	128 (76.2%)	1.27 ± 0.99	1.22 ± 0.89	1.31 ± 1.13	1.40 ± 1.16	0.011*
Fatigue	106 (63.1%)	1.03 ± 0.98	0.86 ± 0.90	1.23 ± 0.96	1.33 ± 1.18	0.023*
Pain	92 (54.8%)	0.86 ± 0.97	0.89 ± 0.90	0.74 ± 1.02	0.93 ± 1.17	0.030*
Muscle weakness	86 (51.2%)	0.82 ± 0.97	0.74 ± 0.91	1.00 ± 0.97	0.87 ± 1.17	0.380
Memory & concentration dysfunction	79 (47.0%)	0.65 ± 0.82	0.61 ± 0.75	0.67 ± 0.81	0.77 ± 1.04	0.201
Lymphedema	56 (33.3%)	0.49 ± 0.79	0.47 ± 0.72	0.46 ± 0.82	0.57 ± 1.01	0.062
Breathing discomfort	39 (23.2%)	0.27 ± 0.53	0.23 ± 0.51	0.28 ± 0.46	0.37 ± 0.67	0.164
Dysphagia	32 (19.0%)	0.24 ± 0.55	0.23 ± 0.51	0.18 ± 0.39	0.33 ± 0.80	0.051
Speech difficulty	31 (18.5%)	0.22 ± 0.50	0.20 ± 0.50	0.23 ± 0.49	0.27 ± 0.58	0.351

The scores are recorded in mean ± SD

The symptoms are scored on a three-point scale

SD standard deviation, *Gp 1* total number of chemotherapy cycle equal to and under 6, *Gp 2* from 7 to 12 cycles, *Gp 3* equal to and more than 13 cycles

*Significant difference among groups of increasing number of chemotherapy cycles was assessed by Kruskal Wallis test ($p < 0.05$)

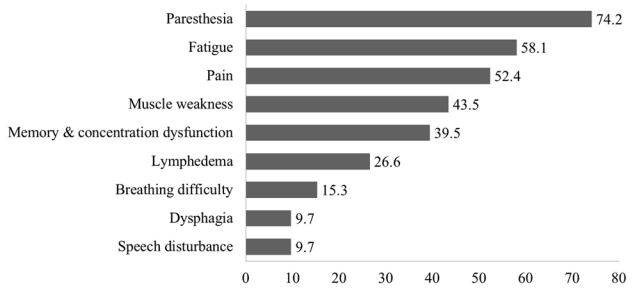

Fig. 1 Prevalence of cancer or cancer treatment-related subjective symptoms in ovarian cancer patients under chemotherapy (%)

increase in the number of chemotherapy cycles contributed to a 0.031 increase ($p < 0.001$) in fatigue.

Functional loss in daily living

The Katz score and dependence of each domain function are described in Table 3. The majority of patients (80.95%) were independent in their activities of daily life with a mean Katz index score of 5.6 out of 6. About 19.05% of total participants showed dependence in ADLs, with the most affected ADL functions being continence, bathing, transfer, and dressing, in descending order. The influence of chemotherapy was shown in majority of the functional domains in ADL. Multivariate regression analysis revealed the number of chemotherapy cycles to be the sole significant factor that influenced total Katz score (Table 4).

Table 3 The number of patients with dependence in function according to the functional domains of Katz index ($N = 168$)

Katz category	Number, *n* (%)	*p* value (coefficient)
Independent	136 (80.95%)	
Partially dependent	26 (15.48%)	
Dependent	6 (3.57%)	
Domain		
Continence	24 (14.3%)	0.022* (− 0.176)
Bathing	11 (6.5%)	0.219 (− 0.095)
Transfer	9 (5.4%)	0.023* (− 0.175)
Dressing	9 (5.4%)	0.163 (− 0.108)
Toileting	6 (3.6%)	0.012* (− 0.193)
Feeding	4 (2.4%)	0.001* (− 0.255)
Total score (mean ± SD)	5.625 ± 1.059	0.060 (− 0.145)

SD standard deviation

*Significant difference according to number of chemotherapy cycles was assessed by Spearman correlation (coefficient) ($p < 0.05$)

Recognition of rehabilitation needs

Among 168 patients, 124 patients completed questionnaires on their awareness of the need for rehabilitation intervention regarding their present symptoms. There was a large discrepancy between the percentage of patients experiencing the cancer and cancer treatment-related symptoms and the percentage of patients recognizing the need for rehabilitation intervention (Fig. 2).

Table 4 Summary of multiple linear regression analysis for variables predicting fatigue and functional loss in ADL ($N = 168$)

Covariates	*B*	SE	*p* value
Univariate models (fatigue)			
Number of chemotherapy cycles	0.032	0.009	0.001*
Recurrence	0.413	0.164	0.013*
Age	0.008	0.007	0.264
Marital status	− 0.161	0.089	0.070
Education status	0.048	0.070	0.495
DM	− 0.032	0.286	0.910
HTN	− 0.039	0.181	0.831
Cancer stage	0.152	0.099	0.127
Multivariate model (fatigue)			
Number of chemotherapy cycles	0.031	0.009	0.001*
Multivariate model (total score of Katz)			
Number of chemotherapy cycles	− 0.044	0.010	0.000*

B regression coefficient, *SE* standard error, *DM* diabetes mellitus, *HTN* hypertension

*Significant difference ($p < 0.05$)

Discussion

The majority (93.5%) of ovarian cancer patients under chemotherapy had treatment-related symptoms, although not severe. The most commonly reported symptoms were musculoskeletal symptoms such as paresthesia, fatigue, pain, and muscle weakness, which are mostly manageable. Except for paresthesia, which is a well-known complication of chemotoxicity, also known as chemotherapy-induced peripheral neuropathy, fatigue was the most commonly reported symptom. Fatigue is noteworthy, as its severity increased proportionately to the number of total chemotherapy cycles, and as it was significantly correlated with the loss of function in ADL. Despite this substantial proportion of ovarian cancer patients experiencing fatigue during chemotherapy, only a minority (less than 20%) of the patients recognized the need for rehabilitation intervention for symptoms (Fig. 2).

About 20% of ovarian cancer patients under chemotherapy had functional dependence in ADLs. The most affected function was continence, with 14.3% of the participants experiencing some impairment. This was a predictable result as incontinence, in either urination or defecation, is a common burdensome side effect of gynecological cancer treatment [14]. For each of the other ADLs such as bathing, transfer, dressing, toileting, and feeding, 2–7% of the participants had trouble in performance. Multiple linear regression analysis revealed that the total Katz score, representing the functional ability in ADL, decreased proportionally to the increase in total number of chemotherapy, meaning that the accumulated number of chemotherapy affected the functional deterioration of the patients in activities of daily life.

Overall, the majority of the patients experienced cancer of cancer treatment-related symptoms, and fatigue was the second most prevalent symptom, which increased in proportion to the total number of chemotherapy cycles. Moreover, although only a minority (19.05%), the patients had functional loss in ADLs, which worsened in proportion to the accumulated number of chemotherapy done. As both fatigue and functional loss in daily activities can be managed through timely and appropriate rehabilitation intervention, early detection and management through appropriate screening for such disability are necessary. To the best of our knowledge, this is the first study to examine the unmet needs in treatment-related symptoms and functional impairment that are amenable to rehabilitation, specifically focused on ADLs of ovarian cancer patients undergoing chemotherapy.

Previous studies reported that 80–99% of cancer patients experienced fatigue during treatment with chemotherapy, radiotherapy, or both [15]. In the present study, more than half of the participants (63.1%) experienced fatigue, which significantly hampered daily living activities including bathing, dressing, toileting, transferring, continence, and feeding activities. This coincides with the results of Curt et al. [16] reporting that most patients with fatigue were unable

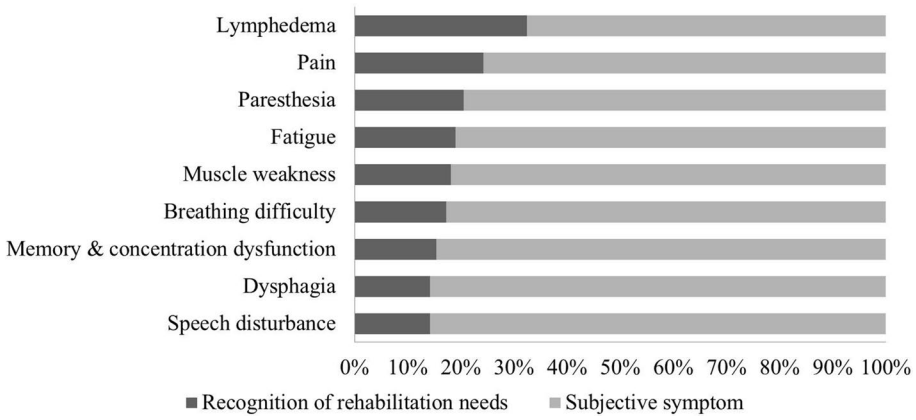

Fig. 2 Discrepancy between subjective symptoms and recognition of rehabilitation needs

to achieve a normal life, and experienced alterations in daily routine. As shown from the regression analysis in the present study (Table 4), the total number of chemotherapy cycles was the primary contributing factor to fatigue symptoms and total score of functional scale (Katz). In other words, the higher the dosage of accumulated chemotherapy, the more the toxicity and fatigue, which also resulted in significant decrease in ADL function. Thus, managing fatigue in ovarian cancer patients undergoing chemotherapy through appropriate rehabilitation intervention is the key to prevent disability in daily living functions. Timely provision and modulation of rehabilitation service may minimize any anticipated increases in symptom burden, especially fatigue, and ameliorate functional limitations.

There have been a number of studies regarding the deterioration of the quality of life in cancer patients. A few of these studies involved ovarian cancer patients undergoing chemotherapy, which is identical to the participants of the present study. Bhugwandass et al. [17] studied 107 early-stage ovarian cancer patients and compared the quality of life of the patients according to the history of adjuvant chemotherapy. Mardas et al. [4] studied 61 ovarian cancer patients undergoing chemotherapy to assess the quality of life. These studies used the same commonly used questionnaire to assess the health-related quality of life for the cancer patients. The questionnaire included questions about the impairment in physical, role, emotional, cognitive, and social functions. Yet, the questions are broad and insufficient for the detailed assessment of functional loss in ADLs to cover the entire rehabilitation spectrum. On the other hand, the Katz index is a valid scale with optimal reliability for the assessment of basic ADLs [18] with a relatively detailed classification of ADL function, which supplements the shortcomings of the previous studies. The present study is the first to focus on the functional loss in ADLs, in addition to the possible treatment-related symptoms of larger number of ovarian patients during their chemotherapy.

However, there were several limitations to the present study. First, the influence of different chemotherapy regimens was not clarified in the study. The classification of chemotherapy according to the different regimens and drugs was omitted in the study. This is due to different regimens used among different medical centers and discordance in the combinations of drugs. Since the regimen protocol was subjected to a change depending on the patients' sensitivity, resistance and toxicity to certain drug, the number of treatments and the regimen varied per individual. Moreover, the previous study of Lakesta et al. assessed the differences in symptoms in relation to the regimen, either cisplatin or carboplatin, and reported no significant difference except for the gastrointestinal symptoms [19]. Thus, the influence of different chemotherapy regimens on symptoms and functional loss in ADLs is expected to be minimal, whereas that of the total number of cycles of treatment was substantial, as determined in the present study. Second, the influence of surgery was not clarified enough in the study. The presence of surgery history either as primary surgery or interval debulking surgery was collected as shown in Table 1. However, due to various surgery types, surgery extents and frequencies, it was hard to be classified and analyzed. We anticipate that further study with sophisticated classification of the surgery and investigation of its influence on patients' symptoms and function in daily life may produce enriched research results.

In conclusion, majority of the patients experienced treatment-related symptoms, especially fatigue, and about 20% of the patients had functional loss during chemotherapy which in turn aggravated in proportion to the accumulated dose of chemotherapy. By identifying the symptoms and loss in ADL function among ovarian cancer patients under chemotherapy, appropriate and timely rehabilitation intervention for symptom relief and functional restoration in ADLs may become feasible. Moreover, as fatigue and functional loss aggravate in proportion to the accumulated chemotherapy cycle, it may be minimized or prevented through rehabilitative intervention, such as regular exercise, for the patients with ongoing multiple cycles of chemotherapy. Future studies on establishment of a qualified and validated screening tool and system for the detection of symptoms and functional loss of cancer patients during chemotherapy could further increase the quality of life for cancer survivors. Moreover, timely assessment followed by referral efforts, not only at the time of cancer diagnosis, but also beyond treatment, and provision of appropriate cancer rehabilitation are expected to contribute to the improvement in quality of life and also in further prolongation of the survival.

Author contributions IYCheong: project development, data analysis, manuscript writing. JSY: data collection, data analysis. SHC: data collection. SYP: data collection. H-JS: data collection, management. J-WL: data collection. JHH (corresponding author): protocol development, manuscript editing.

Compliance with ethical standards

Conflict of interest None. I have full control of all primary data and I agree to allow the journal to review the data if requested.

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