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Impact of lower limb lymphedema on quality of life in gynecologic cancer survivors after pelvic lymph node dissection

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ABSTRACT

Objective: To evaluate the impact of lower limb lymphedema (LLL) on quality of life (QOL) in cervical, ovarian, and endometrial cancer survivors after pelvic lymph node dissection.
Study design: A cross-sectional case-control study was performed using the Korean version of the Gynecologic Cancer Lymphedema Questionnaire (GCLQ-K) and the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30). In total, 25 women with LLL and 28 women without LLL completed both questionnaires.
Results: The GCLQ-K total symptom score and scores for swelling-general, swelling-limb, and heaviness were significantly higher in the LLL group than in the control group. In the EORTC QLQ-C30, the LLL group reported more financial difficulties compared to the control group (mean score, 16.0 vs. 6.0; $P = 0.035$). Global health status was poorer in the LLL group with borderline statistical significance (mean score, 62.7 vs. 71.4; $P = 0.069$). Spearman's correlations suggested that global health status in the EORTC QLQ-C30 correlated with the GCLQ-K total symptom score (in the LLL group, $R = -0.64$, $P = 0.001$; in the control group, $R = -0.42$, $P = 0.027$).
Conclusions: QOL decreases due to LLL-related symptoms and financial difficulty in women with LLL. Well-designed prospective studies are required to confirm these findings.

Introduction

In 2014, gynecologic cancer is expected to account for 11.7% (94,990) of all new cancers and 10.4% (28,790) of all cancer deaths among women in the United States [1]. In Korea, incidence of gynecologic cancer is continuously increasing, especially endometrial cancer and ovarian cancer with the annual percent changes of 6.9% and 1.5%, respectively [2]. For gynecologic cancer, pelvic lymph node dissection (LND) is performed during staging and/or to reduce tumor burden in gynecologic cancer surgeries. Lower limb lymphedema (LLL) is common after pelvic LND as a result of damage to the lymphatic system [3,4]. LLL could limit mobility and daily activity, and have a negative effect on the psychological and social wellbeing [5]. Recently, Beesley et al. reported that 13% of patients treated with endometrial cancer experienced LLL [6]. Our previous study also showed that even in early-stage ovarian cancer cases, about four of every 10 patients reported past and/or current lower extremity edema and related symptoms after surgical staging including pelvic LND [7].

In survivorship planning in gynecologic cancer patients, LLL after pelvic LND is one of the important issues [8]. Gynecologic Oncology Group (GOG) trials are currently underway to elucidate the incidence, natural course, complications, and impact of LLL after primary treatment for gynecologic cancers [9,10]. However, the impact of LLL after pelvic LND on the quality of life (QOL) in gynecologic cancer patients has not been well investigated. Lymphedema and its debilitating effects on QOL have only been extensively assessed in breast cancer survivors, and these studies have focused on uncomfortable symptoms, as well as physical, psychological, and social functioning [11–16].

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Therefore, the aim of the study was to evaluate the impact of LLL on QOL in gynecologic cancer patients after pelvic LND.

Materials and methods

This cross-sectional case-control study was conducted after obtaining the approval by the Institutional Review Board of National Cancer Center (NCCNCS-13-794).

Between October 2012 and January 2013, gynecologic cancer survivors (cervical cancer, ovarian cancer, and endometrial cancer) who visited the outpatient clinic of National Cancer Center were screened for eligibility. Eligibility criteria were the same as in our previously published study which developed and validated of the Korean version of the Gynecologic Cancer Lymphedema Questionnaire (GCLQ-K) [17]. Patients with age over 18 years, who underwent pelvic lymph node dissection in gynecologic cancer surgery, whose interval from surgery to survey was more than 6 weeks, and who agreed with the written informed consent were included. Patients with the following conditions were excluded from this study: edema with unclear cause, active thrombosis, tumors or local infection in their lower extremity, uncontrolled diabetes mellitus, severe cardiac dysfunction, renal insufficiency, and auto-immune vasculitis. Pregnant or lactating patients, alcohol or drug abusers, and long-term users of systemic corticosteroids were also excluded.

Among the 67 gynecologic cancer patients who met these criteria, patients with LLL were identified clinically through physical examination and limb volume measurement by various methods such as perometry, lymphoscintigraphy, magnetic resonance imaging (MRI), and computed tomography (CT) [17,18]. All patients with swollen lower extremities were evaluated using limb sonography or CT venography to exclude deep vein thrombosis. By this way, 33 patients were verified to have LLL, while the remaining 34 patients did not have LLL.

Two individual questionnaires were conducted in telephone survey: the GCLQ-K and the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30). Patients were requested to answer the items, and both questionnaires were completed in 25 out of 33 patients (75.8%) with LLL (LLL group) and in 28 out of 34 patients (82.4%) without LLL (control group).

The Gynecologic Cancer Lymphedema Questionnaire (GCLQ) is a simple, effective, and time-efficient screening method to identify gynecologic cancer patients with lymphedema [19]. The questionnaire consists of a total of 20 items that are distributed over seven symptom clusters: six items for deteriorated physical functioning (weakness and limited movement), four items for numbness, three items for swelling-general, three items for infection-related, one item for heaviness, one item for aching, and two items for swelling-limb. Each item is scored as 0 or 1, which stands for "no" and "yes", respectively, within the previous 4 weeks. The GCLQ was modified and validated for Korean population, and termed GCLQ-K [17].

The EORTC QLQ-C30 was developed to assess cancer patients' general QOL and has been used widely in various studies [20,21]. Integrating 30 items of cancer-specific questions, this questionnaire displays five functional scales (physical, role, emotional, cognitive, and social), three symptom scales (fatigue, pain, and nausea and vomiting), single-items about additional symptoms common in cancer patients (dyspnea, insomnia, appetite loss, constipation, and diarrhea), global health status scale, and the perceived financial difficulties. All of the scales and single-item measures in score with range from 0 to 100. In a functional scale, a high score represents a high/healthy level of function. A high score for the functional and global health status scales represents a high QOL. In contrast, a high score for a symptom scale or single-item means a high level of problems due to a symptom [20,21]. The Korean version of the EORTC QLQ-C30 has been also validated [22], and was used to assess patients' QOL in this study.

Patient characteristics and questionnaire scores between two groups were investigated to determine the differences. Student's t test and Mann–Whitney U test were used to compare continuous variables. Pearson's chi-squared test, Fischer's exact test, and Kruskal–Wallis test were used to compare categorical variables. Spearman's test was used to evaluate correlations between total symptom score or scores of symptom clusters in the GCLQ-K and global health status in the EORTC QLQ-C30 of both groups. R statistical software (version 2.12.) was used for statistical analysis. A P value <0.05 was considered statistically significant.

Results

The clinico-pathologic characteristics of the patients are presented in Table 1. The proportion of cervical cancer, ovarian cancer, and endometrial cancer cases was 48.0%, 24.0%, and 28.0%, respectively, in the LLL group and 39.3%, 46.4%, and 14.3%, respectively, in the control group, without significant differences between the two group ($P = 0.861$). The following factors were not statistically different between the LLL group and the control group: FIGO stage, age at diagnosis (mean, 45.5 vs. 46.9 years), age at the time of survey (mean, 49.5 vs. 51.9 years), and the time interval from diagnosis to survey (mean, 56.0 vs. 62.2 months). All patients of the two groups received pelvic LND at the time of surgeries. Additional para-aortic LND was performed in 64.0% of the LLL group and in 57.1% of the control group ($P = 0.610$). The mean harvested numbers of lymph nodes were 30.6 and 25.0 in the LLL group and the control group, respectively ($P = 0.358$).

Scores of GCLQ-K symptom clusters are shown in Table 2. Total symptom score was higher in the LLL group than in the control group (mean, 5.32 vs. 1.86; $P < 0.001$). Among the seven GCLQ-K symptom clusters, scores for swelling-general ($P < 0.001$), swelling-limb ($P < 0.001$), and heaviness ($P = 0.007$) were significantly higher in the LLL group. However, scores for physical functioning, infection-related, aching and numbness were not significantly different between the two groups.

In the survey of EORTC QLQ-C30 (Table 3), the scores of five functional scales (physical, role, emotional, cognitive, and social), three symptom scales (fatigue, pain, and nausea and vomiting), and five items of symptoms (dyspnea, insomnia, appetite loss, constipation, and diarrhea) were not statistically different between the two groups. However, financial difficulty was more commonly observed in the LLL group than in the control group (mean, 16.0 vs. 6.0; $P = 0.035$). In addition, global health status was poorer in the LLL group with borderline statistical significance (mean, 62.7 vs. 71.4; $P = 0.069$).

Spearman's correlations were performed to determine associations between the results of the GCLQ-K and those of the EORTC QLQ-C30 in the LLL group (Table 4). Global health status of the EORTC QLQ-C30 was associated with total score of the GCLQ-K ($R = -0.64$, $P = 0.001$). Specifically, global health status decreased with increasing scores of physical functioning ($R = -0.46$, $P = 0.021$), swelling-general ($R = -0.56$, $P = 0.004$), and heaviness ($R = -0.48$, $P = 0.014$). Each functional scale of the EORTC QLQ-C30 was associated with symptoms reported in the GCLQ-K.

The results of Spearman's correlations in the control group also showed a correlation between global health status of the EORTC QLQ-C30 and total score of the GCLQ-K ($R = -0.42$, $P = 0.027$) (Table 5). Scores for physical functioning ($R = -0.45$, $P = 0.016$) and numbness ($R = -0.45$, $P = 0.015$) were associated with decreased global health status.