INTRODUCTION

In 2014, ovarian cancer is estimated to comprise 1.7% (2,271) of all new female cancers and to be the eighth leading cause of female cancer deaths in Korea [1]. Due to a lack of effective screening tools, ovarian cancer tends to be diagnosed at an advanced stage and has relatively high recurrence and mortality rates, compared with other gynecologic malignancies [2,3]. For maximal ovarian cancer survival, extensive cytoreductive surgery, and adjuvant chemotherapy are required [4-9]. At the same time, patients’ quality of life (QoL) becomes a major issue among survivors.

Sexuality, or sexual functioning, has been recognized as an important QoL component [10]. Sexuality is a multidimensional concept involving the physical, psychological, and social aspects of an individual’s life [11,12]. Survivors of gynecologic malignancies are at high risk of developing disturbed sexuality owing to the treatment modality, treatment-related advanced stage and has relatively high recurrence and mortality rates, compared with other gynecologic malignancies [2,3]. For maximal ovarian cancer survival, extensive cytoreductive surgery, and adjuvant chemotherapy are required [4-9]. At the same time, patients’ quality of life (QoL) becomes a major issue among survivors.

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genital deformities, and hormonal changes [13,14]. According to previously published studies, more than a half of ovarian cancer survivors frequently experience sexuality changes, including decreased sexual interest, activity, and enjoyment [15-17].

However, heterogeneity in study designs, populations, and survey tools exist among the studies, making their interpretation difficult. Moreover, most of the literature has described deteriorated sexual functioning only among ovarian cancer survivors. Studies comparing the sexuality of survivors with that of healthy women have not yet been reported. Data describing the exact differences between these groups would be clinically informative and useful. Thus, this study compared QoL and sexual functioning between ovarian cancer survivors and healthy women.

MATERIALS AND METHODS

This cross-sectional, case-control study was conducted after the approval by the National Cancer Center Institutional Review Board (NCCNCS-12685).

Among the women who visited the outpatient clinic of National Cancer Center between February 2013 and April 2014, ovarian cancer survivors and healthy women who met the eligibility criteria were enrolled. The eligibility criteria for ovarian cancer survivors were age over 18 years, ability to understand Korean, sexual activity within the previous 3 months, and under surveillance after primary treatment without any evidence of disease. Healthy women were defined as women without any invasive cancer in their medical records, and who had also engaged in sexual activity within the previous 3 months. Women who declined to provide written informed consent were excluded from the study.

Demographic data of the enrolled participants were collected by reviewing medical records and interviewing. The participants were requested to complete three individual questionnaires. Then, propensity score matching was performed to adjust covariates, including age, and marital, educational, economic, and occupational status between ovarian cancer survivors group and healthy women group.

The questionnaires were used to measure QoL and sexual functioning, and included the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30) [18], Ovarian Cancer Module (EORTC QLQ-OV28) [19], and the Female Sexual Function Index (FSFI) [20].

The EORTC QLQ-C30, developed to assess cancer patients’ general QoL, is a 30-item cancer-specific questionnaire. This questionnaire assesses five functional scales (physical, role,
emotional, cognitive, and social), three symptom scales (fatigue, pain, and nausea and vomiting), a scale for global health and overall QoL, single-items regarding additional symptoms commonly reported by cancer patients (dyspnea, insomnia, appetite loss, constipation, and diarrhea), and perceived financial difficulties. The scales and single-item measures are scored from 0 to 100. In the functional and global health scales, higher scores represent better functioning or status. In contrast, higher scores on the symptom scales and for the single-items reflect more problematic symptoms [18].

The EORTC QLQ-OV28 was developed to supplement the EORTC QLQ-C30 for the more specific assessment of ovarian cancer patients’ QoL. It is composed of 28 items, assigned to seven scales, measuring abdominal/gastrointestinal symptoms, peripheral neuropathy, other chemotherapy side effects, hormonal menopausal symptoms, body image, attitude towards disease and treatment, and sexual function. For the symptom and attitude scales, higher scores reflect higher levels of problems. In contrast, high functional scale scores (body image and sexual function) reflect better QoL [19].

The FSFI is composed of 19 items designed to assess sexual functioning in women, with a specific focus on six domains: desire, arousal, lubrication, orgasm, satisfaction, and pain. A higher score in each domain indicates better status [20].

The Korean versions of the EORTC QLQ-C30 and the FSFI have been validated, and were used in this study [21,22]. The Korean translation of the EORTC QLQ-OV28 was available at the EORTC group website (http://groups.eortc.be/qol), and was used with permission.

Statistical analyses were performed to test differences, between the two groups, in patient characteristics and questionnaire scores. The Student t-test and Mann-Whitney U-test were used to compare continuous variables. The Pearson chi-square test, Fisher exact test, and Kruskal-Wallis test were used to compare categorical variables. R statistical software version 2.12 (http://www.r-project.org) was used for the statistical analyses. A p<0.05 was considered statistically significant.

## RESULTS

Among the 257 ovarian cancer patients screened, 103 women

| Table 1. Demographic characteristics of ovarian cancer survivors and healthy women |
|---------------------------------|-------------------|-----------------|-----------------|-------------------|
| Characteristic                  | Ovarian cancer survivors (n=73) | Healthy women (n=73) | p-value |
| Age (yr)                        | 50.7±8.3          | 52.0±7.2        | 0.290           |
| Marital status                  |                   |                 |                 |
| Single/separated/widowed        | 3 (4.1)           | 5 (6.8)         | 0.719           |
| Married                        | 70 (95.9)         | 68 (93.2)       |                 |
| Education                       |                   |                 |                 |
| ≤Middle school                  | 10 (13.7)         | 13 (17.8)       | 0.650           |
| ≥High school                    | 63 (86.3)         | 60 (82.2)       |                 |
| Family income ($/mo)            |                   |                 |                 |
| <2,000                          | 8 (11.0)          | 10 (13.7)       | 0.765           |
| 2,000–4,000                     | 34 (46.6)         | 30 (41.1)       |                 |
| >4,000                          | 31 (42.5)         | 33 (45.2)       |                 |
| Occupational status             |                   |                 |                 |
| Yes                             | 26 (35.6)         | 26 (35.6)       | 0.863           |
| No                             | 47 (64.4)         | 47 (64.4)       |                 |
| Menopause status                |                   |                 |                 |
| Yes                             | 66 (90.4)         | 65 (89.0)       | 1.000           |
| No                             | 7 (9.6)           | 8 (11.0)        |                 |
| Regular exercise                |                   |                 |                 |
| Yes                             | 45 (61.6)         | 41 (56.2)       | 0.614           |
| No                             | 28 (38.4)         | 32 (43.8)       |                 |

Values are presented as mean±SD or number (%).

| Table 2. Clinical characteristics of ovarian cancer survivors (n=73) |
|---------------------------------------------------------------|
| Characteristic | Value |
|----------------|-------|
| FIGO stage     |       |
| I              | 38 (52.1) |
| II             | 7 (9.6)   |
| III            | 24 (32.9)  |
| IV             | 4 (5.5)    |
| Type of treatment |     |
| S only         | 16 (21.9) |
| S+C            | 57 (78.1) |
| Type of surgery |       |
| Laparotomy     | 56 (76.7) |
| Laparoscopy    | 16 (21.9) |
| Convert to laparotomy | 1 (1.4) |
| Lymphadenectomy |       |
| PLND only      | 7 (9.6)   |
| PLND+PALND     | 51 (69.9) |
| Retrieved LN   |       |
| Pelvic         | 18.4±10.8 (0–56) |
| Para-aortic    | 14.8±8.5 (0–37) |

Values are presented as number (%) or mean±SD (range).

C, six cycles of taxane- and platinum-based adjuvant chemotherapy; FIGO, International Federation of Gynecology and Obstetrics; LN, lymph node; PALND, para-aortic lymph node dissection; PLND, pelvic lymph node dissection; S, cytoreductive surgery.
satisfied the eligibility criteria for ovarian cancer survivors group, and 220 women were included in the healthy women group. All women, in both groups, completed the three questionnaires. After propensity score matching, a total of 73 ovarian cancer survivors (study group) and 73 healthy women (control group) were compared in the current study (Fig. 1).

The demographic characteristics of both groups are presented in Table 1. As propensity score matching were performed, the following factors were not statistically different between ovarian cancer survivors and healthy women: age (mean, 50.7 years vs. 52.0 years; \( p=0.290 \)), marital status, education, family income, occupational status, menopause status, and regular exercise. Among the ovarian cancer survivors, the median interval from diagnosis to survey was 38.0 months, with a mean of 56.9 months (range, 5 to 261 months).

Table 2 shows that the proportion of cancer survivors at International Federation of Gynecology and Obstetrics (FIGO) stages I, II, III, and IV were 52.1%, 9.6%, 32.9%, and 5.5%, respectively. Cytoreductive surgery followed by six cycles of taxane- and platinum-based chemotherapy was performed on 78.1% of the ovarian cancer survivors; 21.9% underwent surgery only. During cytoreductive surgery, lymphadenectomy was performed on 79.5% of the survivors; 9.6% received pelvic lymph node dissection only, and 69.9% received both pelvic and para-aortic lymph node dissection. The mean harvested numbers of pelvic lymph nodes and para-aortic lymph nodes were 18.4 and 14.8, respectively.

The results of the EORTC QLQ-C30 and -OV28 questionnaires for both groups are shown in Table 3. In the EORTC QLQ-C30 survey, only the scores for social functioning and financial difficulties were significantly different between the groups, with worse social functioning (mean, 82.4 vs. 90.9; \( p=0.010 \)) and more financial difficulties (mean, 16.4 vs. 7.8; \( p=0.019 \)) being reported by the ovarian cancer survivors than by the healthy

| Table 3. Quality of life comparison between ovarian cancer survivors and healthy women |
|----------------------------------|-----------------|-----------------|-----------|
| Domain                          | Ovarian cancer survivors (n=73) | Healthy women (n=73) | p-value   |
| EORTC QLQ-C30                   |                               |                  |           |
| Physical functioning            | 81.5±11.5                   | 82.3±13.2        | 0.688     |
| Role functioning                | 84.5±17.9                   | 87.7±15.7        | 0.253     |
| Emotional functioning           | 76.4±19.1                   | 78.9±18.5        | 0.421     |
| Cognitive functioning           | 77.6±19.3                   | 78.8±15.8        | 0.696     |
| Social functioning              | 82.4±22.5                   | 90.9±16.2        | 0.010     |
| Fatigue                         | 31.7±18.8                   | 35.2±22.5        | 0.308     |
| Nausea and vomiting             | 8.0±15.0                    | 6.6±12.0         | 0.543     |
| Pain                            | 15.8±18.6                   | 18.7±22.2        | 0.383     |
| Dyspnea                         | 8.2±14.5                    | 11.4±18.6        | 0.249     |
| Insomnia                        | 23.7±25.7                   | 26.0±27.9        | 0.608     |
| Appetite                        | 6.4±14.3                    | 9.1±16.9         | 0.293     |
| Constipation                    | 25.1±27.7                   | 21.9±27.9        | 0.488     |
| Diarrhea                        | 7.8±18.0                    | 10.0±19.8        | 0.467     |
| Financial difficulties          | 16.4±25.5                   | 7.8±18.0         | 0.019     |
| Global health status            | 65.4±21.5                   | 62.6±20.2        | 0.411     |
| EORTC QLQ-OV28                  |                               |                  |           |
| Body image                      | 67.8±28.9                   | 74.9±20.6        | 0.091     |
| Sexuality                       | 40.9±19.5                   | 44.6±20.6        | 0.301     |
| Attitude to disease             | 49.5±27.9                   | 62.1±20.4        | 0.002     |
| Abdominal/GI symptoms           | 19.8±15.4                   | 17.8±15.3        | 0.443     |
| Peripheral neuropathy           | 25.7±22.7                   | 20.1±15.9        | 0.085     |
| Hormonal menopausal symptoms    | 20.5±19.9                   | 20.1±20.4        | 0.891     |
| Other chemotherapy side-effects  | 21.5±16.5                   | 20.6±14.5        | 0.735     |

Values are presented as mean±SD.
EORTC QLQ-C30, The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; EORTC QLQ-OV28, The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Ovarian Cancer Module; GI, gastrointestinal.
In the EORTC QLQ-OV28, the attitude towards disease and treatment score was significantly lower, suggesting a better attitude in the ovarian cancer survivor group than in the healthy women group (mean, 49.5 vs. 62.1; \( p=0.002 \)). Meanwhile, the other six scales (abdominal/gastrointestinal symptoms, peripheral neuropathy, other chemotherapy side effects, hormonal/menopausal symptoms, body image, and sexual function) were not statistically different between the two groups (\( \text{Table 3} \)).

In the sexuality comparison, all the six domains (desire, arousal, lubrication, orgasm, satisfaction, and pain) of the FSFI were not statistically different between the two groups; neither were the total FSFI score (mean, 19.9 vs. 20.8; \( p=0.489 \)) (\( \text{Table 4} \)). The sexual function scale of the EORTC QLQ-OV28 was subdivided into individual items (interest in sex, sexual activity, enjoyment of sex, and dry vagina) and compared between the two groups. Only vaginal dryness was more problematic in the ovarian cancer survivor group, compared with the healthy women group, having borderline statistical significance (\( p=0.081 \)) (\( \text{Table 4} \)).

### DISCUSSION

In the current study, we showed that sexuality was not impaired in ovarian cancer survivors who did not show evidence of disease after primary treatment and had engaged in sexual activity, compared with healthy women.

Sexual dysfunction may occur due to several aspects of ovarian cancer treatment. Surgery, including oophorectomy, causes menopause in premenopausal women, and results in decreased estrogen and androgen production. The decreased hormonal production results in vaginal atrophy, vaginal dryness, dyspareunia, frequent urinary tract infections, hot flashes, mood swings, and irritability. Chemotherapy also influences the patient’s general condition by causing, for example, increased fatigue. Psychological factors also contribute to sexual problems. Depression and anxiety decrease sexual desire, and hysterectomy and abdominal scarring may distort an individual’s body image [23-25].

According to Stewart et al. [15], more than half (57%) of ovarian cancer survivors reported that the cancer and its treatment worsened their sexual functioning. In advanced stage ovarian cancer (FIGO stages III and IV), decreased sexual interest was reported in 31% of survivors, and decreased sexual activity was observed in 46% of survivors [16]. Even in early stage (FIGO stages I and II), Matulonis et al. [17] reported that the proportions of survivors with an interest in sexual relations, and those involved in sexual activity were only 10%, and 9%, respectively. However, in the current study, statistical difference were not observed between the study and control groups with regards to their sexuality; the total scores and the scores for each of the six FSFI domains (desire, arousal, lubrication, orgasm, satisfaction, and pain), and the individual items relating to sexual function in the EORTC QLQ-OV28 (interest in sex, sexual activity, enjoyment of sex, and dry vagina) were similar.

The discrepancy in the results, compared with previous studies, may be explained by one or more of the following possibilities. First, the eligibility criteria for the study populations were different among the studies. In the current study, early and advanced stage diseases were not considered separately; 61.6% and 38.4% of the ovarian cancer survivors were early (FIGO stages I and II) and advanced (FIGO stages III and IV) stage disease, respectively. Second, the time intervals between diagnosis and the survey were different among the studies. Third, the proportion of women excluded due to the absence of recent sexual activity was also much higher among ovarian cancer survivors (140 out of 257, 54.5%) than among the healthy women (28 out of 267, 10.5%). This observation may be explained by the tendency of gynecologic cancer survivors to be more reluctant to engage in sexual activity because of a fear that sexual activity might increase the risk of disease recurrence [26]. Lastly, as Asians are considered to be more sexually conservative than Western populations, Korean women generally show low levels of sexual interest and activ-

| Domain                  | Ovarian cancer survivors | Healthy women | \( p \)-value |
|-------------------------|--------------------------|---------------|--------------|
| Interest in sex         | 33.3±24.9                | 33.3±24.2     | 1.000        |
| Sexual activity         | 31.1±22.5                | 33.3±23.6     | 0.550        |
| Enjoyment of sex        | 41.6±35.0                | 49.8±40.1     | 0.189        |
| Dry vagina              | 67.1±37.1                | 78.1±38.2     | 0.081        |

**Values are presented as mean±SD.**

EORTC QLQ-OV28, The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Ovarian Cancer Module; FSFI, The Female Sexual Function Index.

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ity, possibly counterbalancing the differences between the groups [27].

Thus, although sexuality was similar between the groups, sexual problems among survivors should be considered and properly managed during treatment time and surveillance. For example, despite showing borderline statistical significance (p=0.081), vaginal dryness was more problematic for ovarian cancer survivors than for healthy women. This symptom may be improved by applying vaginal lubricants and/or local estrogen cream.

In QoL comparison between the two groups, we also found that components of the EORTC QLQ-C30 and -OV28 were not different between ovarian cancer survivors and healthy women, except with respect to social functioning, financial status, and attitude towards disease. It is well known that both the surgery and chemotherapy have negative impacts on ovarian cancer patients’ QoL [28]. Nevertheless, according to the previously published studies, QoL may improve significantly throughout the treatment period, particularly after completion of chemotherapy [29,30]. In a longitudinal study, significant improvements in the EORTC QLQ-C30 questionnaire were also associated with continued survival [31].

In a recent prospective study which examined survivors’ QoL 10 years posttreatment using the same questionnaire, the long-term survivors showed similar QoL scores compared with the reference group [32].

However, worse social functioning in the study group, compared with controls, suggests that recovery of social functioning may be retarded compared with other functions. Although financial conditions were not precisely evaluated, we can predict that the survivors incurred treatment-related costs that may have influenced their financial situation. Additionally, long-term cancer survivors frequently experience work changes, such as unemployment, during treatment [33,34]. Interestingly, better disease-specific attitudes among ovarian cancer survivors might reflect the survivors’ confidence and optimism regarding their disease after having endured difficult treatment, overcome the disease, and successfully achieved a disease-free status.

Despite efforts to clarify eligibility criteria and to adjust covariates using propensity score matching between the two groups, there were several limitations to this study. First, as a cross-sectional, case-control study design, some selection bias is inevitable. Second, as clinical data were collected using self-reported patient surveys, questionnaire-related issues may exist. Third, during propensity score matching, not all possible confounding factors were considered. Fourth, impact of lymphadenectomy was not evaluated. Impact of pelvic lymph node dissection-related nerve injury on sexuality was needed to be investigated in near future. Lastly, the ovarian cancer survivors might have undergone different types of surgery (for example, low anterior resection or Hartmann’s operation for bowel surgery), resulting in different side effects; surgical details were not collected in this study.

In conclusion, this study suggests that sexuality was similar between health women and ovarian cancer survivors who were without evidence of disease and having sexual activity. However, the study group did demonstrate deteriorated social functioning and financial status, compared with controls. Further prospective cohort studies are warranted. Especially, as only sexually active cancer survivors were included in the current study, the studies elucidating factors that hinder ovarian cancer survivors from having sexual activity are necessary to completely understand sexuality issues affecting ovarian cancer survivors and to provide clinically informative advice.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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