RESEARCH ARTICLE

Quality of Life in Ovarian Cancer Patients Choosing to Receive Salvage Chemotherapy or Palliative Treatment

Manasawee Srisuttayasathien*, Nipon Khemapech

Abstract

**Background:** The hypothesis that patients who primarily progress on two consecutive chemotherapy regimens without evidence of clinical benefit may opt for supportive care was investigated. The purpose was to determine the quality of life in recurrent ovarian cancer patients choosing to receive salvage chemotherapy in addition to supportive care or palliative care alone. A secondary objective was to evaluate factors that affect quality of life in ovarian cancer patients. **Materials and Methods:** A descriptive study was conducted in patients who had histological confirmed epithelial ovarian cancer and failed to respond to at least one regimen of chemotherapy, coming for treatment at the King Chulalongkorn Memorial Hospital in Bangkok, Thailand over a six-month period from August 2012-March 2013. Each patient was asked to complete the FACT-G and a general personal questionnaire. The median quality of life score was analyzed. The Mann Whitney U Test was used to compare the difference between salvage chemotherapy and palliative care groups, and the Kruskal Wallis was used to evaluate other variables. **Results:** Thirty-eight ovarian cancer patients were identified who failed to respond to at least one regimen of chemotherapy. Of the 38, 30 chose salvage chemotherapy and eight palliative care for further treatment. By histology the carcinomas were predominantly endometrioid subtype and poorly differentiated. The majority of patients in this study had FIGO stage III, and ECOG status 0-1. The median quality of life score was 76.3 (35.8-94.0), with no significant differences between the groups. Factors associated with the quality of life were the ECOG score and number of chemotherapeutic courses. **Conclusions:** In the setting of refractory or recurrent epithelial ovarian cancer, patients who receive salvage chemotherapy have comparable quality of life scores with patients treated with palliative care alone, providing a contrast with previous studies.

**Keywords:** Quality of life - ovarian cancer - salvage chemotherapy - palliative care

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Introduction

Ovarian cancer is the leading cause of death of women worldwide. Because ovaries are intra-abdominal organs, and as there is still no effective screening tool for ovarian cancer, the majority of patients who present are in the advanced stages of the disease (Carter et al., 1997). Surgical exploration is necessary to obtain tissue for histologic study, staging, and hopefully for optimal surgery. Combination chemotherapy with carboplatin and paclitaxel is the adjuvant treatment of choice for patients with high-risk disease. Therapy of refractory and recurrent ovarian cancer aims to palliate symptoms and improve quality of life. For platinum-sensitive, recurrent ovarian cancer, patients preferred combination chemotherapeutic regimens including carboplatin/paclitaxel, carboplatin/weekly paclitaxel, carboplatin/docetaxel, carboplatin/gemcitabine, carboplatin/liposomal doxorubicin, or cisplatin/gemcitabine. Possible chemotherapeutic regimens for platinum-resistant disease include topotecan, gemcitabine, liposomal doxorubicin and etoposide. Patients who primarily progress on two consecutive chemotherapeutic regimens without evidence of clinical benefit may be offered supportive care, additional therapy, or clinical trials, which should be made on a highly individual basis (NCCN, 2013). However, the side effects of the salvage treatment may be a significant cause of distress and excessive disability. Physical complication and side effect have significant impact on ovarian cancer survivors’ psychological health (Roland et al., 2013). Since the treatment is usually aggressive, some patients choose to deny salvage chemotherapy.

For matters related to health care, quality of life has applied specifically to those life concerns that are most affected by health or illness, hence the term “health-related quality of life” (HRQL) (Up to date, 2012). HRQL is a multidimensional concept that refers to how an individual’s usual physical, emotional and social well-being are impacted by a medical condition and its treatment (Von Gruenigen et al., 2010). Because HRQL information can provide a detailed assessment of disease and treatment effects and their global impact on the individual’s daily life, it can be used as a planning tool for assessing the need for further treatment, rehabilitation
or palliative care (Up to date, 2012). The Thai version of the Functional Assessment of Cancer Therapy-General (FACT-G) is a multidimensional questionnaire developed and validated for cancer patients. It would be interesting to determine whether salvage therapy and palliative care alone affect quality of life. The FACT-G scores for 870 ovarian cancer patients were calculated in one study, as follows: mean(SD) of physical well-being=24.19 (3.90), functional well-being=21.01 (5.15), emotional well-being=19.62 (3.54), social well-being=19.68 (5.28), and global FACT-G=82.14 (13.18) (Wilailak et al., 2011).

Some studies have clearly shown a positive effect on HRQL when cancer salvage treatment was provided. On the contrary, Carter et al. (1997) reported no significant alterations on HRQL when prolonged chemotherapy was administered. Patnaik et al. (1998) found that the role of chemotherapy in advanced ovarian cancer was effective in improving quality of life in at least half of the patients, even though only approximately one fourth of patients had an objective response to their disease. Macquart-Moulin et al.(2000) showed that HRQL deterioration disappeared after completion of cancer treatment and that the patients were usually able to return to a level of physical functioning consistent with that of their pre-cancer diagnosis. On the other hand, studies have revealed that more consideration should be given to improving HRQL during therapy. Hamilton, (1999) reported that the frequently used multimodality treatment strategy often predisposed women to depression and heightened anxiety. Greimel et al. (2002) concluded that global HRQL, emotional functioning, and role-functioning remained low throughout the course of disease, up to one year after completion of treatment. Doyle et al.,(2001), who observed the smallest benefit of palliative chemotherapy with a score of 6.6% on a seven-point scale for the physical function and 2.2% for the global QL question. According to the National Comprehensive Cancer Network (NCCN, 2013), in conditions in which patients had progressive disease during primary chemotherapy or stable disease or relapse within six months after primary chemotherapy, they could be offered treatment with second-line chemotherapy or supportive care only, which were both standard treatments for these groups of patients. One observational study found quality of life did not significant increase or decrease, following commencement of second-line chemotherapy in platinum-resistant disease (Beesley et al., 2013). Generally, the response to second line chemotherapy was approximately 15-35 percent (Berek, 2011) and the median overall survival was documented at about nine months with treatment (Grzankowski et al., 2011). While a focus on the cost effectiveness of treatment is important, for beneficence, the choices of treatment should concentrate on patients’ autonomy and their quality of life (Patnaik et al., 1998). Two Asian studies suggested the quality of life improvement can be achieved by effective symptom management, especially by alleviating emotional distress (Wang et al., 2010; Cheng and Yeung, 2013).

Although previous studies in developed countries reported that ovarian cancer patients tend to have reduced quality of life, this issue has never been assessed and compared between patients who receive salvage chemotherapy and palliative care alone in recurrent situations especially in Thailand, which has different cultural and traditional values than western countries. The goal of this study is to evaluate quality of life in recurrent ovarian cancer patients, in patients given salvage chemotherapy in addition to supportive care and in patients given only palliative care. We are hopeful that our study will help clinicians make appropriate decisions regarding effective treatment for ovarian cancer patients.

Materials and Methods

We administered a questionnaire for epithelial ovarian cancer patients treated at King Chulalongkorn Memorial Hospital over a six month period with failure of at least one regimen of chemotherapy. Thirty-eight ovarian cancer patients were recruited after counseling regarding the choice of treatment. Thirty patients chose salvage chemotherapy while eight patients chose only palliative care.

Additional requirements for inclusion in this study were age 20-75 years, literate in Thai language, Eastern Cooperative Oncology Group (ECOG) performance status 0-3, adequate laboratory results including, hematologic count: leukocyte count >4,000 cells/mL, platelets >150,000 cells/mL, liver function: total bilirubin <1.2 mg/dL, serum amino transferase <160 IU/L and kidney function: creatinine clearance >90 mL/min/1.73m².

Women were excluded if there was a diagnosis of psychiatric disorder, mental retardation or communication deficits; if they had two primary cancers or metastatic cancer to the ovaries, or if they were found to have other serious medical diseases or organ dysfunctions.

The choice of chemotherapy regimen was chosen by the treating physician. In our King Chulalongkorn Memorial Hospital, generally a platinum-based regimen was used for platinum-sensitive diseases. In patients who did not respond to first-line carboplatin or with recurrence within a disease-free interval of less than six months, possible regimens include topotecan, gemcitabine,

<table>
<thead>
<tr>
<th>FACT domains</th>
<th>Chemotherapy Median (min-max)</th>
<th>Palliative Median (min-max)</th>
<th>Overall Median (min-max)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical</td>
<td>18.50 (5.00-27.00)</td>
<td>14.00 (10.00-24.00)</td>
<td>18.00 (5.00-27.00)</td>
</tr>
<tr>
<td>Role</td>
<td>19.40 (14.00-28.00)</td>
<td>22.65 (12.00-26.80)</td>
<td>19.90 (12.00-28.00)</td>
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<tr>
<td>Emotional</td>
<td>20.00 (10.00-24.00)</td>
<td>18.00 (12.00-24.00)</td>
<td>19.50 (10.00-24.00)</td>
</tr>
<tr>
<td>Social</td>
<td>19.50 (8.00-28.00)</td>
<td>14.00 (8.00-23.00)</td>
<td>19.00 (8.00-28.00)</td>
</tr>
<tr>
<td>Global(tot)</td>
<td>77.40 (35.80-94.00)</td>
<td>69.30 (52.80-94.00)</td>
<td>76.33 (35.80-94.00)</td>
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*p-value is based on the Mann Whitney U test

liposomal doxorubicin and etoposide. If the patients have recurrence after six months, platinum-based regimens could be given to them.

The choice to maintain chemotherapy or palliative care was chosen by the patient. History, physical examinations, tumor markers and imaging were performed and confirmed both progressive and recurrent disease. All of the patients were offered maintenance chemotherapy. The aims of therapy were explained to the participants, that chemotherapy may benefit in improving quality of life, relieving symptoms and slowing progression of the disease, but was not being used for curative reasons. Some of our patients chose palliative care alone. Palliative care consisted of analgesics, nutritional support, abdominal paracentesis if indicated, blood transfusions to correct severe anemia and psychosocial-family support.

As a means to identify additional potential participants for the study, each patient was asked to i) identify other potential participants according to inclusion/exclusion criteria; ii) contact them by word-of-mouth and briefly explain the survey; and iii) send the questionnaires to potentially eligible subjects.

**Questionnaires**

The questionnaires were composed of two parts: i) The general personal questionnaire, consisting of questions related to demographic characteristics and clinical data. ii) The Thai version of Functional Assessment of Cancer Therapy (FACT-G), version 4.

The Thai version of FACT-G in this study has been granted license by the FACIT organization, tested for reliability and validated for use with Thai people. It consists of 27 questions made up of four subscales: physical well-being (0-28 points), social/family well-being (0-28 points), emotional well-being (0-24 points), and functional well-being (0-28 points). The total potential score ranges between 0-108. The higher the score indicates the better the QOL.

As they did the questionnaires, patients could refuse to answer any question whenever they felt uncomfortable. If the patient had symptoms of major depressive disorder, we considered a psychiatrist consultation. Reliability of the questionnaires by a pilot study was tested in 15 ovarian cancer patients in King Chulalongkorn Memorial Hospital and calculated for reliability values (internal consistencies). The Cronbach’s alpha statistic was 0.828.

**Statistical method**

SPSS program for Windows, version 17 was used to sort data and analyse the reliability and the results of the questionnaire. To determine the sample size, an estimation for continuous data was performed (Wilalak et al., 2011). Descriptive statistics such as median, minimum, maximum, and frequencies were used to determine a quality of life score. To evaluate the significance of the difference between salvage chemotherapy and palliative care groups, the Mann Whitney U Test was calculated. The Kruskal Wallis test was used to investigate other variable factors that affect patients’ quality of life.

**Results**

Thirty-eight ovarian cancer patients who had recurrence or were refractory to at least one regimen of chemotherapy were treated at King Chulalongkorn Hospital and calculated for reliability values (internal consistencies). It consists of 27 questions made up of four subscales: physical well-being (0-28 points), social/family well-being (0-28 points), emotional well-being (0-24 points), and functional well-being (0-28 points). The total potential score ranges between 0-108. The higher the score indicates the better the QOL.

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Most of them had International Federation of Gynecology and Obstetrics stage III and poorly differentiated carcinoma (grade 3). The endometrioid subtype had the longest time since therapy, with a range from 2-5 years. For the majority of women in this study ECOG performance status was 0-1.

From Table 2, the median of global quality of life score in recurrent ovarian cancer was 76.33 (35.80-94.00). The median of physical, role, emotional and social well-being domains were 18.00 (5.00-27.00), 19.90 (12.00-28.00), 19.50 (10.00-24.00), and 19.00 (8.00-28.00), respectively.

The comparison of quality of life between the chemotherapy and palliative alone groups was analyzed using the Mann Whitney U test. According to our study, there were no statistical differences between the patients who received salvage chemotherapy group and the patients who were treated with palliative care alone p=0.229, 0.244, 0.829, 0.67 in physical, role, emotional, and social domains respectively.

Factors associated with quality of life were analyzed using the Kruskal Wallis test; the dependent variables were global FACT-G scores. The ECOG score, number of chemotherapeutic cycles and time since therapy were significantly related to patients’ quality of life (p=0.04, 0.03 and 0.04 respectively).

The global FACT-G scores of patients with ECOG scores 0 and 1 were significantly higher than those with scores 2 and 3. The median of quality scores were (min-max) 81.40 (60.20-94.00) and 78.15 (52.80-92.00) vs. 58.90 (35.80-79.00) and 65.55 (56.30-71.60) in patients with ECOG scores 0-1 and 2-3, respectively.

On the other hand, the number of chemotherapy cycles was positively associated with the quality of life scores. The patients who received two courses of chemotherapy had lower quality of life than those who received three and four or more courses: The median quality of life score (min-max) in patients who received two courses was 72.30 (35.80-93.00) vs 81.15 (65.00-93.00) for those with three cycles, and 81.95 (64.80-94.00) for those who received greater than four courses.

Furthermore, there was a positive association between global quality of life score and time since therapy. The results were the same as for the numbers of courses: the patients who had been treated for two years and more after diagnosis had higher quality of life than who had been treated less than two years: Median quality of life scores were (min-max)=78.00 (52.80-94.00) vs 66.30 (35.80-93.00) in patients treated for two years and more, and less than two years, respectively.

There were no statistical differences between other variables and global FACT-G score. Table 3 illustrates the correlation of the variables and total quality of life scores.

**Discussion**

It has been generally accepted that quality of life is one of the major goals for treatment in recurrent ovarian cancer patients. However, physicians seem not to be concerned about it during salvage treatment and patients continue to receive salvage chemotherapy repeatedly regardless of the benefit.
There have been very few studies regarding quality of life in ovarian cancer patients. Wilalak et al. (2011) studied FACT-G scores in 870 ovarian cancer patients. They found mean (SD) domains of 24.19 (3.90), 21.01 (5.15), 19.62 (3.54) and 19.68 (5.28) in physical well-being, functional well-being, emotional well-being and social well-being, respectively and global FACT-G of 82.14 (13.18). Another study of the use of additional chemotherapy in the setting of recurrent situations found modest benefit in score 6.6% on a seven-point scale for the physical function and 2.2% for the global QL question (Doyle et al., 2001).

Our study found the median of the global quality of life score in recurrent ovarian cancer was 76.33 (35.80-94.00). The median of physical, role, emotional and social well-being domains were 18.00 (5.00-27.00), 19.90 (12.00-28.00), 19.50 (10.00-24.00), and 19.00 (8.00-28.00), respectively. These seem to be lower than previous reports that studied general ovarian cancer patients. Furthermore, we found no differences in quality of life scores between patients who received salvage chemotherapy and the patients who were treated with palliative care alone, which is different from the study of Doyle et al.(2001). This may be due to the difference of culture, tradition, nationality and life style of the patients recruited and also the chemotherapeutic regimen used in the studies.

In relation to the quality of life variables, our study found that patients’ performance status (ECOG) was inversely correlated with quality of life scores. A higher score indicated a poorer status. The patients who were unable to carry out any work activities (ECOG =2) and who were more than fifty percent bedridden (ECOG =3) had significantly lower quality of life score than those of fully active status (ECOG=0) and those who were symptomatic but complete ambulatory (ECOG=1).

Furthermore, our study found that numbers of chemotherapy courses are positively associated with the quality of life scores. The patients who received more chemotherapy courses had higher quality of life scores. This may be explained that the patients who had been diagnosed for two years or more lived longer after the first diagnosis and gradually coped with the cancer during chemotherapy treatments; these findings possibly indicate that the disease progressed slowly and was less aggressive than the patients who were diagnosed for less than two years. However, further studies are still needed to provide more conclusive findings.

The distinctive point of our study is that it is the first study to determine the quality of life in recurrent ovarian cancer patients and compare two groups receiving salvage chemotherapy and palliative care alone. The comparable outcome between the two groups may be advantageous for developing countries in terms of diminishing their expenses of treatment of recurrent ovarian cancer patients. However, the weak points of our study are the limited number of patients and selection bias. Patients who are fit enough are likely to select salvage chemotherapy treatment and the patients who are too weak to receive salvage chemotherapy may choose palliative care alone. However it is difficult to do a randomized trial study equitably because of ethical issues.

This study may provide important data for further studies comparing cost effectiveness between salvage chemotherapy and palliative treatment in recurrent ovarian cancer patients and this will have impact on recommendation for management in these groups of patients especially in a developing country.

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