Determinants of Quality of Life in Ovarian Cancer Survivors: A Pilot Study

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Abstract

- **Objective:** Ovarian cancer treatments and outcomes vary substantially, yielding a diverse group of survivors. Few data exist on quality of life (QoL) concerns and the foremost needs of these patients. Our goal was to conduct a pilot study to determine the QoL needs of ovarian cancer survivors to establish priorities for future interventions.
- Methods: In this cross-sectional study, the European Organization for Research and Treatment of Cancer Quality of Life Questionnaires (EORTC QLQ-C30 and OV28) QoL questionnaires and one investigator-derived questionnaire were administered in an outpatient setting. Clinical parameters were abstracted and tested for associations with QoL measures.
- Results: A total of 102 women consented to participate and completed all components. Their mean age was 58 years (range 29 to 85), with 80% having epithelial ovarian carcinoma and 66% highgrade serous carcinoma. Women with stage I (28%), II (15%), III (47%), and IV (10%) lesions were represented in the primary treatment (25%), surveillance (46%), recurrent (23%), and palliative (7%) phases of the survivorship continuum. Fifty-one percent characterized their disease burden as "quite a bit" or "very much," and this did not vary by histology or diagnoses. Global QoL did not vary by clinico-pathologic parameters. Cardiovascular and respiratory comorbidities were associated with EORTC scores in physical functioning (P = 0.027 for cardiovascular and P = 0.041 for respiratory), global QoL (P = 0.03 for cardiovascular and P = 0.039 for respiratory), and sexual health (P = 0.025 for cardiovascular). Task completion/memory/concentration, anxiety, and fatigue were the distress categories given highest priority by respondents.
- **Conclusion:** In women with ovarian cancer, clinical factors such as age, stage, and histology did not have a significant impact on QoL. Psychosocial factors have a larger impact on global QoL than physical symptoms.

Key Words: Survivorship, ovarian cancer, quality of life, EORTC QLQ-C30, OV-28 Competing Interests: None declared. Received on December 27, 2013

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Résumé

- **Objectif**: Les traitements contre le cancer de l'ovaire et leurs résultats varient considérablement, il en résulte donc un groupe diversifié de survivantes. Nous ne disposons que de peu de données sur les questions liées à la qualité de vie (QdV) de ces patientes et sur leurs besoins les plus criants. Nous avions pour objectif de mener une étude pilote visant à déterminer les besoins des survivantes du cancer de l'ovaire en matière de QdV afin d'établir les priorités pour ce qui est des futures interventions.
- Méthodes : Dans le cadre de cette étude transversale, les questionnaires sur la QdV de la *European Organization for Research and Treatment of Cancer Quality of Life Questionnaires* (EORTC QLQ-C30 et OV28) et un questionnaire formulé par les chercheurs ont été administrés au sein d'une clinique externe. Les paramètres cliniques ont été résumés et analysés en vue d'y déceler des associations avec les mesures de la QdV.
- Résultats : Au total, 102 femmes ont consenti à participer à l'étude et ont rempli toutes les composantes requises. Leur âge moyen était de 58 ans (plage : de 29 à 85); 80 % d'entre elles présentaient un carcinome épithélial de l'ovaire et 66 % présentaient un carcinome séreux de haut grade histologique. Les femmes présentant des lésions de stade I (28 %), de stade II (15 %), de stade III (47 %) et de stade IV (10 %) étaient représentées dans les phases « traitement primaire » (25 %), « surveillance » (46 %), « récurrent » (23 %) et « palliatif » (7 %) du continuum de la survie. Cinquante et un pour cent des répondantes ont caractérisé le fardeau de la maladie comme étant « plutôt lourd » ou « très lourd » et cette façon de répondre ne variait pas en fonction de l'histologie ou du diagnostic. La QdV globale ne variait pas en fonction des paramètres clinico-pathologiques. Des comorbidités cardiovasculaires et respiratoires ont été associées aux scores EORTC en ce qui concerne le fonctionnement physique (P = 0,027 pour ce qui est des comorbidités cardiovasculaires et P = 0.041 pour ce qui est des comorbidités respiratoires), la QdV globale (P = 0,03 pour ce qui est des comorbidités cardiovasculaires et P = 0,039 pour ce qui est des comorbidités respiratoires) et la santé sexuelle (P = 0,025 pour ce qui est des comorbidités cardiovasculaires). L'incapacité d'achever une tâche / les troubles de la mémoire et de la concentration, l'anxiété et la fatigue figuraient parmi les catégories de détresse auxquelles les participantes ont accordé la priorité absolue.

Conclusion : Chez les femmes qui présentent un cancer de l'ovaire, des facteurs cliniques tels que l'âge, le stade et l'histologie n'exerçaient pas un effet significatif sur la QdV. Les facteurs psychosociaux exercent un effet plus important sur la QdV globale que les symptômes physiques.

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INTRODUCTION

In 2006, the Institute of Medicine released *From Cancer Patient to Cancer Survivor: Lost in Transition.*¹ This sentinel report called for dramatic changes in the way care is provided for cancer survivors. It emphasized that cancer care should extend beyond primary treatment to include long-term care that addresses physical, psychosocial, and emotional factors that influence survivors throughout their lifetime. From this call to action, research in survivorship has grown, but survivorship data in women with ovarian cancer are inconsistent and limited.²

Ovarian cancer is a diverse disease, with a wide range of prognoses depending on factors such as the patient's age, performance status, histological subtype, stage at presentation, residual disease left at the time of surgery, BRCA status, and treatment received.³⁻¹³ Because of these variables, a patient may be told she has anywhere from a 10%to a greater than 95% five-year survival rate,^{10,13,14} making the available survivorship data difficult to generalize. Even in patients with advanced high-grade serous cancer (in which recurrence is the norm), chemotherapy response rates are favourable; multiple treatment regimens can be administered over a patient's lifetime, achieving a relatively long-term survival. In addition, the traditional view of epithelial ovarian cancer as a single disease is slowly evolving to a view that encompasses a group of diseases (high-grade serous, low-grade serous, endometroid, clear cell, and mucinous carcinoma), all which have different epidemiology, genetic risk factors, molecular events, premalignant lesions, patterns of spread, response to chemotherapy, and prognosis.^{15,16} With this diversity, it is unknown whether survivorship issues are generalizable for all ovarian cancer survivors.

ABBREVIATIONS

C30	Core Questionnaire
EORTC	European Organization for Research and Treatment of Cancer
GI	gastrointestinal
OV	Ovarian Cancer Module
QLQ	Quality of Life Questionnaire
QoL	quality of life

In addition, many patients with cancer have at least one medical comorbidity and the interplay of other chronic diseases and cancer can be complex,^{17–19} affecting treatment (e.g., choice of drug, dose), side effects, quality of life, and the course of the cancer itself.²⁰ In order to interpret QoL data for an individual we must determine what is due to the cancer, what is due to treatment, and what are sequelae from a pre-existing condition, and how or if these factors interact.

Prior QoL investigations in survivors of ovarian cancer have often focused on only one time period (e.g., primary treatment) or only one aspect (e.g., neuropathy). An approach that captures the range of needs among survivors in all stages of the ovarian cancer survival continuum is needed.²¹ Given the diversity of this disease, we cannot extrapolate findings from studies of survivors of prostate or breast cancer, of which there is a relative abundance.^{19,22} Although there is overlap between all cancer survivors, ovarian cancer survivors have a disease-specific range of survivorship concerns (such as bowel obstruction or peripheral neuropathy) that warrant investigation.²³

It is well established that support and appropriate interventions not only improve the perspectives of patients and their families but may also affect an individual's overall survival.^{24–27} The primary objective of our pilot study was to obtain baseline QoL data for ovarian cancer survivors at our regional cancer centre to guide support services for these patients, to reallocate resources to address patient need, and to enable the measurement of QoL improvements or degradation for future interventional trials by establishing a baseline status. Given the diverse nature of ovarian cancer, we hypothesized that survivorship needs would vary by histologic subtype, age, stage, stage in treatment, and underlying comorbidities.²⁸

MATERIALS AND METHODS

We invited all women with a diagnosis of ovarian cancer attending the outpatient gynaecologic oncology followup clinic in our cancer centre to participate in our study. This site serves as the main referral centre for our province and neighbouring territory, with centralized surgical care yielding a large regional variation in population. Recruitment began in January 2012 and was completed in May 2012. The inclusion criteria were:

- 1. having the ability to read and write English,
- 2. having the ability to fully understand the study procedures and give informed consent,
- 3. being over the age of 18, and

4. having had a diagnosis of ovarian cancer of any stage (including borderline tumours) and having undergone treatment with surgery, chemotherapy, or radiation.

Our sample size was based on internal data from our centre to ensure that we obtained a full range of ages, prognoses, and diagnoses among participants. There are approximately 315 new cases of ovarian cancer diagnosed each year in British Columbia²⁹; of these, 85% are epithelial ovarian cancer, 5% to 7 % germ cell, and 5% to 10% sex-cord stromal. Of the cases of epithelial ovarian cancer, 70% are high-grade serous, 10% each clear cell and endometrioid, 4% mucinous, 6% low-grade serous, and 4% other.^{30,31} Using regional statistics, we concluded that a sample size of 100 participants would encompass women across a wide age range and with variable prognoses. A total of 196 patients were approached, with 53% uptake, leading to a study cohort of 102 patients. All participants provided written informed consent.

For evaluation, we used the European Organization for Research and Treatment of Cancer Quality of Life Questionnaires (EORTC QLQ-C30 and OV28).32,33 Both are validated and standardized questionnaires that have been widely used in assessing QoL in women with ovarian cancer.^{2,33-35} We also administered an investigator-derived questionnaire that assessed access to technology and resources and attempted to address survivorship needs versus symptoms (online eAppendix). Both paper and online versions of the questionnaires were made available. The EORTC QLQ-C30 and OV28 online version was developed through collaboration with the EORTC^{32,33} and the Computer-based Health Evaluation Software from Innsbruck Medical University.36 The online version of the investigator-derived questionnaire was administered through the Zoomerang survey program.³⁷

Participants were offered the opportunity to complete the QoL surveys before or immediately after their clinical visits. Questionnaires were completed in written format, in computer tablet or desktop electronic format, or in verbal format with research staff. Survey data from all patients were ultimately entered electronically (via the Computerbased Health Evaluation Software and Zoomerang Programs^{36,37}) to aid in analysis. Objective clinical and treatment data were abstracted from patient charts and entered into a Microsoft Excel database (Microsoft Corp., Redmond WA) after the questionnaires were completed. Clinical data recorded included clinical tumour stage; histology; recurrence; treatment regimens; comorbidities including pre-existing psychiatric diagnoses such as depression or anxiety disorder; medications; hereditary testing; and performance status.

The EORTC QLQ-C30 and OV-28 scales were linearly transformed to a continuous scale (0 to 100) according to the scoring EORTC scoring procedures.³⁴ Higher scores on the functioning scales and the global QoL/health status scales indicated a higher level of functioning, and higher scores on the symptom scales were associated with increased severity of symptoms. The median statistic was chosen as the primary reporting measure of the QoL data because a significant proportion of the data had a skewed distribution; we felt therefore that the median would serve as a more robust measure of central tendency and would be less influenced by outliers. Descriptive statistics were used to quantify the QoL parameters in the EORTC questionnaires and the investigator-derived questionnaire. One-way analysis of variance was conducted to determine the impact of clinical parameters on QoL. All data were analyzed using JMP v10.0 (SAS Institute, Cary, NC). As this was a pilot study, no corrections were made for multiple comparisons, and consequently P values < 0.05were considered statistically significant.

Ethics approval for the study was provided by the British Columbia Cancer Agency Research Ethics Board.

RESULTS

The characteristics of participants are shown in Table 1. The mean age of our population was 58 years, with 80% of patients having epithelial ovarian tumours and 66% of those having high-grade serous histology. Fifty-four percent of participants were undergoing active treatment, and 46% were undergoing surveillance. The median time since diagnosis was 20 months. Ninety-five percent of participants had obtained a high school diploma or higher, and 96% had access to a computer a home. The majority of participants (86%) underwent primary surgical treatment, 74% received platinum/taxane chemotherapy for a median of six cycles. Radiation treatment was involved in the primary adjuvant treatment of 10% of participants. Comorbidities, abstracted from medical charts, were as follows: 38% of participants had cardiovascular disease, 8% had diabetes, 9% had a history of deep vein thrombosis or venous thromboembolism, and 14% had a diagnosis of mental illness.

Overall, the global QoL reported by participants was a median of 66.6 with an interquartile range of 56.3 to 83.3 (Table 2). This was lower than the scores in the functional scales for the QLQ-C30. Of the QLQ-C30 functioning components, the cognitive metric had the largest degradation, with a median score of 75; this contrasted with the physical metric, which had a median score of 86.7. Of the QLQ-C30 symptomatic components, insomnia, pain, and fatigue were

the major QoL detriments, with median scores of 33.3, 16.7, and 33.3, respectively. Symptom scales on the OV-28 instrument indicated higher median scores for body image (75), attitude to disease and treatment (55.6), chemotherapy side effects (22.2), and peripheral neuropathy (22.2).

We asked participants to rank their level of distress (none, some, moderate, significant, or extreme) for a variety of survivorship issues (online eAppendix). Responses were dichotomized to "no distress" or "any distress" to quantify the population at risk for QoL degradation. Participants reported anxiety (76%), fatigue (71%), and task completion/ memory (72%) as the most distressing issues (Figure). When asked to prioritize the issues in order of importance to be addressed by care providers, the participants listed task completion/memory, anxiety, and fatigue.

Univariate analysis was conducted comparing the symptom and functioning scales with clinical factors such as age, stage, histology, and stage in treatment and with comorbidities including cardiovascular, respiratory, gastrointestinal, renal, and other. Predictably, older participants were more affected by chemotherapy (P = 0.042) and had greater peripheral neuropathy (P = 0.024). Emotional functioning was associated with disease stage (P = 0.023); those with stage II ovarian cancer had better emotional functioning than those with stage III disease. Fatigue was also associated with disease stage (P = 0.026); women with stage II disease had less fatigue than those with stage III.

Global QoL was affected by stage in treatment; those undergoing active treatment had a lower QoL (P = 0.040). In addition, undergoing active treatment was associated with more severe scores for nausea and vomiting (P = 0.018), constipation (P = 0.020), abdominal/GI discomfort (P = 0.016), and chemotherapy side effects (P = 0.024). Additionally, those with cardiovascular and respiratory comorbidities had a decreased global QoL (P = 0.031 and 0.040, respectively).

We also asked participants about their preferred method of sharing their QoL experiences. Eighty-two percent preferred to participate using written questionnaires, compared with 8% favouring in-person interviews and 10% favouring electronic methods or tablet computer. Ninety-five percent of participants had computer access at home, and 70% described using a computer daily.

DISCUSSION

The demographic measures and baseline QoL scores from this pilot study are in keeping with QoL reports from other assessments in a mixed ovarian cancer population.^{27,38–41} Table 1. Patient characteristics

Table 1. Patient characteristics	
Characteristic N = 102	Participants, n (%)
Age, years, mean (range)	58 (29 to 85)
Ovarian tumour histology	
Epithelial ovarian	82 (80)
Sex cord stromal	5 (5)
Borderline	15 (15)
Stage in treatment	
Primary treatment	25 (25)
Surveillance after primary	37 (36)
Recurrence	23(23)
Surveillance post-recurrence	10 (10)
Palliative	7 (7)
Stage	
I	29 (28)
II	15 (15)
III	48 (47)
IV	10 (10)
Time since cancer diagnosis, months (n = 98)	
Mean	46
Standard deviation	141
Median	20
Epithelial ovarian cancer histology (n = 82)	
High-grade serous	54 (66)
Low-grade serous	3 (4)
Endometroid	10 (12)
Clear cell	9 (11)
Mucinous	5 (6)
Transitional cell	1 (1)
Cancer treatment	
Primary surgery	86 (89)
Delayed primary surgery	8 (8)
Chemotherapy	72 (74)
Radiation	10 (10)
Comorbidities	
Diabetes	8 (8)
Mental illness	14 (14)
History of VTE/PE	9 (9)
Cardiovascular	37 (38)
Respiratory	11 (11)
Renal	6 (6)
Current medications	
Pain	23 (23)
Sleep aid	26 (27)
Anti-emetics	27 (28)
VTE/PE: Venous thromboembolism/pulmonary embolism	

Table 2. Univariate analysis c	of clinico-	-pathologic paramete	rs and qua	lity of life							
EORTC QLQ-C30/OV-2	28—Unadji	sted scores*				Univ	/ariate ANO/	A/			
			luO)	y significant	P values shor	(uv		Corr	norbidities		
QOL Measures	z	Median score (IQR)	Age	Stage	Histology†	Stage in Treatment	5	Respiratory	ত	Renal	Other
QLQ-C30											
Global QoL, n = 94	94	66.6 (56.3 to 83.3)				0.040	0.031	0.040			
Functional scales‡							0.028	0.041			
Physical functioning	96	86.7 (73.3 to 93.3)						0.050			
Role functioning	97	83.3 (50 to 100)									
Emotional functioning	94	83.3 (66.7 to 100)		0.023							
Cognitive functioning	94	75 (58.3 to 91.7)									
Social functioning	94	83.3 (66.7 to 100)									
Symptom scales§											
Fatigue	97	33.3 (22.2 to 47.2)		0.026							
Nausea and vomiting	97	0 (0 to 16.7)				0.018					
Pain	96	16.7 (0 to 33.3)						0.007			
Dyspnea	97	0 (0 to 33.3)						0.001	0.012		0.011
Insomnia	97	33.3 (0 to 66.7)									
Appetite loss	97	0 (0 to 33.3)									
Constipation	96	0 (0 to 33.3)				0.020		0.014			
Diarrhea	94	0 (0 to 0)									
Financial difficulties	94	0 (0 to 33.3)									
QLQ-0V28											
Symptom scales§											
Abdominal/GI	96	19.0 (9.5 to 33.3)				0.016					
Peripheral neuropathy	96	22.2 (2.8 to 41.7)	0.024								
Hormonal	96	16.7 (0 to 66.7)									
Body image	94	75 (50 to 100)									
Attitude to disease/treatment	94	55.6 (33.3 to 66.7)									
Chemotherapy side effects	96	22.2 (11.1 to 33.3)	0.042			0.024					
Sexual function	93	0 (0 to 25)					0.025				
*Scores range from 0 to 100.											
†Histology—epithelial ovarian cancer or	rly (includes	: clear cell, endometroid, muci	nous, high-gra	de and low-gr	ade serous).						
#Higher values indicate improved function	oning.										
SHigher values indicate worsening sym	ptoms.										
Higher values indicate improved functi	on. Scaling p	performance has not been est	ablished.								
IOR internuartile range. CV cardiovasc	ular										



Symptom distress scales among ovarian cancer survivors

However, comparisons between studies are fraught with difficulty because of overall small sample sizes,^{38,40} treatment-specific or stage-specific studies,^{41,42} and the use of other QoL instruments.^{43,44} The usefulness of these pilot data is in the provision of overall trends in a mixed population and the identification of priority issues in survivorship. In particular, the OV28 parameters of body image and attitude to disease and treatment had median scores of 75 and 55.6, respectively; this is a significant area of concern when other physical symptoms such as peripheral neuropathy and chemotherapy side effects had lower scores of 22.2 (Table 2). Why this finding was so prominent is difficult to explain, because many factors contribute to body image and attitude; nevertheless, it does warrant further exploration.

To better understand these differences in QoL, we undertook univariate analysis to examine factors known to be associated with improved survival in women with ovarian cancer (such as age, stage, histology, and comorbidities). We found that there was no major difference in QoL outcomes according to cancer stage and other traditional clinico–pathologic factors, a finding which is supported by the current survivorship literature.^{39,41} A sub-analysis was also undertaken examining QoL parameters according to whether the participant had active disease or was undergoing surveillance; we found that symptom-related factors were significantly higher in the former, but overall global quality of life and functional scales were unchanged. On balance, ovarian cancer survivors report emotional symptoms, negative feelings about treatment/prognosis and body image, and fatigue as their main concerns. This suggests that psychosocial factors may have a greater effect on QoL than the physical sequelae of cancer.³⁹

There are several limitations to our study. First, this was a pilot study with a relatively small number of participants. However, our patient numbers and overall findings were similar to those of studies in other centres, suggesting that there are similarities in survivorship issues across regions and cultures.^{2,39} In addition, the aim of this pilot study was to identify general trends rather than to undertake definitive hypothesis-testing, and statistically significant associations should therefore be interpreted in this context. Secondly, we had a mixed population with varied histology and with different stages of treatment and remission. Our findings likely underestimate the true effects on quality of life with a uniform patient population (i.e., with aggressive or advanced stage disease). However, this mixed population is a true representation of the ovarian cancer population in our province's largest cancer centre and will serve as a baseline for future population studies. Surprisingly, there were more similarities than differences across these diverse diagnoses, which make the study themes more striking. Other factors affecting survivorship that were not assessed in our study included patient involvement in decision-making; we also did not conduct a detailed exploration of psychiatric illness, which may also play an underlying role.⁴⁵

We are aware of the limitations of self-administered questionnaires developed by clinicians,⁴⁶ and we therefore kept the investigator-derived basic questionnaire separate from the statistical analyses of the EORTC questionnaires. The data obtained by this questionnaire would otherwise be irretrievable because the data it contains are not routinely collected at patient visits. In planning the next phases of support (i.e., consideration of survivorship care plans), many practical aspects must be understood in this population. In addition, there is continued discussion of the relative importance of "symptoms," which are assessed by the physician, versus "needs" as reported by the patient (also known as patient reported outcomes) and as we begin to appreciate the importance of patient preference greater weight must be given to what patients identify as priorities.

CONCLUSION

Ovarian cancer survivors in British Columbia report that psychosocial factors, such as fatigue, anxiety, and cognitive function cause the greatest distress for them and are areas of priority for survivorship interventions. Further, we found that these issues of concern do not correlate with clinical predictors of improved treatment outcomes, such as age, tumour stage, grade, and histology. Underlying comorbidities, however, do affect overall quality of life and should be addressed in a patient's follow-up plan. Our findings suggest that survivorship interventions may be delivered as one entity (inclusive of psychological, physical, and social parameters) and not focused specifically on a given clinical parameter (e.g., neuropathy alone). Because we have obtained baseline quality of life data in ovarian cancer survivors in British Columbia against which the success or failure of future directives can be measured, we will work to translate the knowledge gained from this initiative into effective interventions in the province.

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