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Chapter 2

Quality of Life in Ovarian Cancer Treatment and Survivorship

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Additional information is available at the end of the chapter

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1. Introduction

The past two decades have witnessed an unprecedented level of attention devoted to the assessment of Quality of Life (QOL) in cancer patients. This is a result of a major change that occurred in the way cancer management and its impact has been understood and practiced. Contrary to earlier views, which focused primarily on prolonging the quantity of life of the patient, cancer management recognizes now the potential effects of the diagnosis and treatment on the overall functioning and well-being of the patient. QOL issues and its measurement became particularly important in oncology throughout the different phases of the cancer trajectory. In this context, the National Cancer Institute (NCI) has recommended that cancer research focus on both survival and QOL [1]. Many instruments have been developed and used in clinical and research settings. It is noteworthy the inclusion of QOL as one of the main endpoints in important randomized clinical trials [2]. The benefits of studying QOL outcomes are evident. Primarily, QOL measurement has the potential to provide information to guide clinical decision making [3]. The knowledge about the impact of the illness and its treatment on cancer patients can help clinicians and patients to make decisions regarding treatment options and choose appropriate supportive therapy adjusted to the patient's needs. The toxicity and tolerability of a given treatment can be as important as its efficacy, as is the ability to help decrease or prevent associated toxicities that have a negative impact on QOL [4]. Furthermore, QOL data can foster patient-clinician interactions in routine practice, identify problems that have a significant impact on QOL, prioritize problems, develop interventions to deal with these problems and evaluate the impact of palliative and rehabilitative efforts [5]. Additionally, it can help to shape public policy and health care decisions made by governmental and private institutions [6] and allow the economic evaluation of healthcare provision [7].

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When considering ovarian cancer in particular, researchers follow the general trend by regarding QOL as one of the most important outcomes. Several reasons make the study of QOL in ovarian cancer patients especially worthy and relevant. First, ovarian cancer is an aggressive illness which is associated with very poor survival and high recurrence rates. It is the most fatal malignancy of the female genital tract and the fourth most common cause of female cancer death [8]. Generally, it is detected at an advance stage, with a 5-year survival rate of 46% for all the stages and 31% for advanced stages [8]. The management of ovarian cancer normally includes radical pelvic surgery and multiple aggressive courses of chemotherapy. The stress of receiving the diagnosis of such an aggressive and life threatening illness, which can be unexpected for many women, may be associated with uncertainty and anxiety about the future. This may be regarded as an immediate threat to a woman's life and an associated fear of death. Additionally, women may suffer disease-related symptoms, which may be very difficult to cope with. These include weight loss, bloating and ascites, fatigue and pain. Women may also experience a wide range of sequalae related to their treatment that do not dissipate with time and may persist for a long-term period [9, 10]. Examples include neutropenia, body distortion, hair loss, bowel and bladder incontinence, loss of taste and appetite, premature menopause, infertility, decrease physical functioning, poor sleep, edema and sexual problems [9, 10]. Another burden involves the amount of time spend in treatments that is lost from family and work [11]. Second, research carried out, specifically, with ovarian cancer patients has shown that a substantial proportion of women experience psychological disorders. Anxiety, depression [9, 12-16] and Post-Traumatic Stress Disorder (PTSD) [17] have been found among different studies. Reports have also highlighted the occurrence of impairments in physical, vocational, social, familial and sexual functioning. Those are not confined to the diagnosis and treatment periods, but have been also observed in short and long-term ovarian cancer survivors. Lastly, advances in Medicine fuelled the development of new treatments for ovarian cancer. However, these treatments have associated side-effects and toxicities that may impact on the QOL of the women. Therefore, when considering a treatment plan, risks and benefits must be balanced in order to achieve an optimal QOL [11]. Improvements in survival in ovarian cancer have been relatively reduced [18]. The ability of chemotherapeutic regimens in slowing the progression of disease to prolong life with active disease has been responsible for those improvements in survival [19]. Undoubtedly, QOL is a fundamental consideration for patients with ovarian cancer.

This chapter addresses the most recent knowledge regarding the impact of the treatment on QOL of ovarian cancer patients. Additionally, QOL in ovarian cancer survivors is also discussed.

2. Quality of life: Brief overview

Central to this particular subject, is the question: What is QOL? Although, it is somehow consensual by the clinical and research communities the importance of studying QOL, it is much less consensual what exactly QOL means. This lack of consensus fuels the appearance

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of different definitions and, inevitably, means of measurement. This makes difficult the comparison of findings among studies and to establish more definite conclusions. Issues of definition and measurement continue to be, in fact, the subject of ongoing debate. Despite lack of consensus in its definition, it is widely accepted that QOL is a multidimensional construct that includes several important dimensions (any area of behavior or experience) [4, 7, 20, 21]. These encompass physical functioning (physical well-being, mobility, ability to perform self-care activities, physical activities, role activities such as work or housework, appetite, comorbidities, fatigue/sleep, symptoms, side-effects), cognitive and psychological functioning (emotional well-being, anxiety, depression, coping, perceptions, prior experience, enjoyment, optimism), social functioning (family interactions, time with friends, leisure activities), disease and treatment related symptoms (such as pain and fatigue), spiritual or existential concerns, sexual functioning, body image, patient's satisfaction with health care, control of the disease [7, 21]. According to the WHO [22], QOL is defined as 'an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. It is a broad ranging concept affected in a complex way by the person's physical health, psychological state, level of independence, social relationships, and their relationships to salient features of their environment". Following these lines, QOL includes all aspects of the individual well-being and must be evaluated from the individual's perspective.

When QOL is considered in the context of health, it is often referred to as health-related QOL (HRQOL). HRQOL is a more specific concept, which reflects the effect of the illness and illness treatment on general well-being. Bowling defined HRQOL as ‘optimum levels of mental, physical, role (e.g. work, parent, career, etc) and social functioning, including relationships, and perceptions of health, fitness, life satisfaction and well-being. It should also include some assessment of patient´s level of satisfaction with treatment, outcome and health status and with future prospects. It is distinct from QOL as a whole, which would also include adequacy of housing, income and perceptions of immediate environment’ [23]. HRQOL is a dynamic concept, as health status deteriorates, experiences, roles and relationships change [24]. Furthermore, It may be modified by impairments, functional status, perceptions, and social opportunities and may be influenced by disease, treatment, and policy [25].

Particularly in ovarian cancer literature, the term QOL is much more extensively used instead of HRQOL. In general, QOL assessment in ovarian cancer patients has been focusing more on the acute phase of the treatment. Of interest is the evaluation of QOL under treatment conditions in randomized clinical trials, focusing on different treatment options. The measurement of QOL in screening and early diagnosis of ovarian cancer is very scarce. It of note that, in fact, screening and early detection of ovarian cancer are very limited in clinical practice, existing narrow useful technologies to assist in early diagnosis. The majority of the QOL measurement in ovarian cancer screening evaluates populations at high risk, such as women with genetic mutations undergoing risk-reducing salpingo-oophorectomy [26]. However, for individuals undergoing risk-reducing salpingo-oophorectomy, screening is more a process of early detection or diagnosis rather than a true screening test [26]. Regard-

ing survivorship, recently, there is a growing interest in the study of QOL in ovarian cancer survivors. The following section focuses on the instruments designed to capture QOL that are more commonly used in this specific population.

3. Measurement of QOL in patients with ovarian cancer

Many instruments have been developed and validated to capture important QOL issues in cancer patients. These instruments comprise four main groups: generic measures of QOL (used to assess non-cancer medical patients), cancer condition-specific (used in general cancer populations), cancer site and treatment-specific instruments. QOL measures are often supplemented by questionnaires designed to evaluate specific dimensions of QOL, for example depression. The use of generic questionnaires allows comparisons of QOL among conditions [7]; however, they lack specificity necessary to understand particular problems inherent to a specific condition, such as cancer. This specificity can be found when disease – and site-specific instruments are used. These are more likely to be responsive to change but are not comprehensive [7]. The Medical Outcome Study (Short Form) MOS SF-36 [27] is an example of a QOL generic instrument used in oncology. The European Organization for Research and Treatment of Cancer QOL Core Questionnaire (EORTC QOL-C30) [28] and the Functional Assessment of Cancer Therapy – General (FACT-G) [20] are examples of condition (cancer) specific instruments. All are self-administered questionnaires, multidimensional, relatively brief, acceptable to patients and have good psychometric properties [7]. The EORTC QOL-C30 and the FACT-G comprise ovarian cancer modules that constitute examples of site specific QOL instruments.

Particularly in ovarian cancer, the most commonly used measures are the EORTC QOL-C30 and the FACT-G [18]. The EORTC QOL-C30 and the FACT-G have a similar format: a core QOL questionnaire applicable to cancer patients in general and specific modules, applicable to specific cancer sites. These instruments have been developed primarily from research environments; however, they will be extremely helpful if they assist physicians in detecting clinically significant differences or changes in a patient condition.

3.1. EORTC QOL-C30

This cancer-specific questionnaire was developed by the Study Group on Quality of Life from the European Organization for Research on Treatment of Cancer comprising a core set of questions applicable to all cancer patients and modules to be used to specific cancer sides, such as ovarian cancer [28, 29]. This instrument was designed to be used in international randomized clinical trials. It is based on a multidimensional model of QOL, covering cancer-specific symptoms of the disease, psychological distress, treatment side-effects, social interaction, physical functioning, body image, sexuality, global health and QOL, and satisfaction with medical care. The core QOL instrument is composed by 30 items, comprising nine scales of QOL: one global QOL scale (2 items), five functional scales (physical functioning, role functioning, cognitive functioning, emotional functioning, social functioning) (15 iems),

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three symptom scales (fatigue, pain, nausea and vomiting) (7 items), and six single items, assessing additional symptoms commonly reported by cancer patients (breathlessness, difficulty sleeping, appetite loss, constipation, diarrhea, and financial difficulties). Each scale is scored separately. Seven questions have a dichotomous yes/no response. For the two global QOL items, respondents have to answer by using a 7-point scale, where '1 = very poor' and '7 = excellent'. The remaining questions have a four-point Likert scale, ranging from '1 = Not at all' to '4 = Very much'. No timeframe is specified in the seven dichotomous questions. In the remaining questions, the patient has to answer according to the past week. Each dimension score for each patient is the sum of that patient's item responses for that dimension, transformed, so that the minimum possible value is zero and the maximum possible value is 100. Each scale has a limited set of possible values, determined by the number of items and the range of response options for each item. For the functional scales and the global QOL scale, a higher score corresponds to a better QOL. For the symptom scales and the single items, a higher score indicates more frequent and/or intense symptom experience and thus a lower QOL. Finally, there are two items that ask respondents to rate their overall physical condition. The EORTC QOL-C30 has established reliability and validity [28]. This scale is easy to complete, acceptable to patients and has been translated into several languages. The EORTC QOL-OV28 is the ovarian cancer module designed to supplement the EORTC QOL-C30, for the assessment of QOL in ovarian cancer patients in clinical trials and related studies. It consists of 7 subscales and a total of 28 items, which assess abdominal symptoms (abdominal pain, feeling bloated, clothes too tight, changed bowel habit, flatulence, fullness when eating, indigestion), peripheral neuropathy (tingling, numbness, and weakness), other chemotherapy related side effects (hair loss and upset by hair loss, taste change, muscle pain, hearing problem, urinary frequency, and skin problem), hormonal/menopausal symptoms (hot flushes and night sweat), body image (less attractive, dissatisfied with body), attitude to disease and treatment (disease burden, treatment burden, and worry about future) and sexual functioning (interest in sex, sexual activity, enjoyment of sex and dry vagina) [29, 30]. Each scale is scored separately. For symptom scales, a higher score means a lower QOL, while for function scales, such as body image and sexual function, a higher score means a better QOL. The EORTC QOL-OV28 is a valid and reliable measure to be used in ovarian cancer populations [30].

3.2. FACT-G

The FACT-G was developed by Cella et al to evaluate QOL in oncology settings [20]. This is the core scale of the instrument system and consists of four dimensions, comprising a total of 27 items. The dimensions include functional well-being (7 questions), emotional well-being (6 questions), social/family well-being (7 questions) and physical well-being (7 questions). These four dimensions can be analyzed separately or aggregated to produce a total QOL score. Response categories for all items range from 0 (not at all) to 4 (very much). Higher scores are associated with increased satisfaction with QOL. The timeframe for this instrument is the past 7 days. FACT-G is tested and validated in large international samples, showing reliability, validity and responsiveness to change over time [20]. This instrument is commonly used in ovarian cancer clinical trials and it is available in many languages. The

supplement of the FACT-G with a set of twelve items specific to ovarian cancer is referred as the Functional Assessment of Cancer Therapy – Ovarian (FACT-O). Items include stomach swelling, losing weight, bowels control, vomiting, hair loss, appetite, appearance, getting around, feeling like a woman, stomach cramping, interest in sex and concerns about ability to have children. The ovarian cancer specific subscale assesses severity of problems that can be targeted by proper disease management. The FACT-O is a valid instrument to be used in ovarian cancer patients [31]. This questionnaire has been commonly used in clinical trials and other descriptive studies. The FACT-O can be used alone or in combination with other scales or subscales of the FACT, such as the FACT/GOG neurotoxicity subscale, or the Anemia (FACT-An) or Fatigue (FACT-F) subscale, if the research interest is these specific issues. The physical well-being and the functional well-being scales of the FACT-G plus the ovarian cancer subscale can be combined to represent the Trial Outcome Index (TOI). This index has excellent psychometric properties [31].

4. Quality of life in ovarian cancer patients

How is the QOL of ovarian cancer patients? Do patients with ovarian cancer experience a good QOL? These are questions that researchers have been attempting to answer in the many studies available dedicated to this subject. The number of studies carried out increased significantly in recent years [18], and collectively, these studies captured ongoing issues and concerns resulting from the ovarian cancer diagnosis and treatment [9]. However, there is a difficulty in drawing definite conclusions to answer the above questions. This is due to the lack of consistency in the types and format of QOL data collected in ovarian cancer patients [18]. The accumulated knowledge about QOL issues in patients undergoing treatment and in survivors of ovarian cancer is presented below.

4.1. QOL during ovarian cancer treatment

The management of ovarian cancer generally requires a multimodal approach. Surgery has always been the cornerstone, which plays an essential role in both diagnosis and treatment. The aim of which is to leave no residual deposits greater than 1–2 cm in diameter. In cases of apparent early stage disease, proper surgical management involves comprehensive surgical staging. Advanced-stage disease frequently requires aggressive surgical debulking [32]. The standard approach is to follow surgery by either intravenous or intraperitoneal chemotherapy. Two classes of cytotoxic components, the plantinums and the taxanes are key components of chemotherapeutic regimens for advanced disease [33]. Both treatment modalities can impact negatively on the QOL of patients [34]. In recurrent disease, a variety of treatment regimens are used, including re-treatment with a platinum and/or taxane agent, and second line agents such as liposomal doxorubicin, topotecan, and gemcitabine. Chemotherapy side effects may be temporary (e.g. hair loss, nausea and vomiting) or cumulative and/or permanent (e.g. fatigue, neurotoxicity) [34].

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It is paramount to understand how ovarian cancer and its treatment may disrupt the overall well-being and QOL of patients. A recent systematic review and meta-analysis, carried out to assess and summarize QOL data before, during and after chemotherapy among ovarian cancer patients, found that baseline QOL may significantly improve, particularly after completion of chemotherapy treatment [18]. Authors identified a total of 139 studies; of those, 48 were randomized clinical trials. However, it was only possible to synthesize data from a subset of studies, due to inconsistencies in the way the data was reported across studies. Pooled data showed that QOL as measured by the EORTC QOL C-30 was found to improve during the treatment period and ovarian cancer specific concerns as measured by the FACT-O subscale, were improved during the treatment period [18]. The EORTC QOL C-30, FACT-G and FACT-O found significant improvements in QOL after completion of primary therapy, despite the lack of measurable improvements during treatment as measured by the FACT-G [18]. Following these lines, a recent longitudinal study evaluated the course of QOL, depressive symptoms, anxiety symptoms and fatigue over the course of chemotherapy until 6 months follow-up [35]. Results demonstrated a significant improvement of QOL, as measured by the EORTC QOL C-30 and EORTC QOL OV-28, from the start of chemotherapy and post-surgery period (QOL was severely impaired and high levels of anxiety symptoms, depressive symptoms and fatigue were found), until after care (symptoms reach nearly general population symptom levels). Although, this was a small study of 23 patients, it highlighted the importance of understanding QOL over the course of treatment [35]. Similar results were obtained by other investigators, reporting improvements of QOL in ovarian cancer during chemotherapy until one year follow-up. Von Gruenigen et al [36] in a sample of 42 ovarian cancer patients found that QOL, as measured by the FACT-G and SF-36, markedly decreased after surgery with a slow improvement during adjuvant chemotherapy, mainly in the physical, functional and fatigue domains. Physical functioning decreased during chemotherapy but increased to perioperative levels following treatment. Functional well-being increased following chemotherapy, while emotional and social scores did not change over time [36]. Collectively, these findings highlight that, in addition to chemotherapeutic treatments, surgery may have a negative impact on QOL. Although several factors may influence this impact, tumour stage, and therefore, the extent of the surgical intervention and the existence of intra – or postoperative complications may be crucial [35]. Minig et al [37] found in a study of 181 women with gynaecological cancers, of which 116 had ovarian cancer, that postoperative complications, surgical complexity, advanced stage were associated with lower levels of postsurgical QOL specifically in ovarian cancer patients. The strongest predictor of postsurgical QOL was preoperative QOL, closely followed by surgical complications. Investigators stressed that postoperative complications may be difficult to avoid due to the aggressiveness of the surgery performed in order to achieve maximum cytoreduction in ovarian cancer; however, attention needs to be paid intraoperatively and postoperatively to the early detection of complications to optimize QOL whenever possible in this group of patients [37]. Consequences of surgery are well documented, including loss of fertility, sexual dysfunction, surgical menopause and bowel obstruction. For women at reproductive age, premature menopause and loss of fertility may be devastating [34].

Several clinical trials evaluating ovarian cancer treatments have been carried out, in which QOL is one of the outcomes evaluated. Table 1 describes recent clinical trials that have included QOL as an outcome. QOL measurement in clinical trials has been useful to argue in favor or against novel therapies. Furthermore, there is some evidence demonstrating that QOL is a prognostic indicator for treatment outcomes [26] and future survival [38-41].

Study	Comparison Group	QOL measures	QOL findings
GOG-172[42]	Intraperitoneal (IP) versus intravenous (IV) therapy for first line therapy	FACT-TOI Neurotoxicity and abdominal discomfort subscales	During active treatment, patients on IP had more QOL disruptions when compared to IV therapy
SCOTROC[43]	Carboplatin docetaxel compared with carboplatin paclitaxel for first line therapy	EORTC QOL-C30 EORTC QOL-OV28	Global QOL scores did not differ between treatment arms. Less neurotoxicity was found in the docetaxel group
Vergote (2010)[44] a Gynecologic Cancer Intergroup Collaboration Trial	Neoadjuvant chemotherapy versus primary surgery in stages IIIC or IV	EORTC QOL-C30 EORTC QOL-OV28	No differences in global health scores
OVAR 3[45]	Cisplatin/paclitaxel versus carboplatin/paclitaxel for first line therapy	EORTC QOL-C30	Higher QOL with carboplatin/paclitaxel
Ferrandina (2008)[46] Multicenter Italian Trials in ovarian Cancer group	Pegylated doxorubicin versus gemcitabine for progressive or recurrent disease	EORTC QOL-C30	Higher QOL in the pegylated doxorubicin arm
OV-05[47]	Early versus delayed treatment for recurrent disease	EORTC QOL-C30	QOL decreased shorter in the early treatment arm; significant disadvantages in role, emotional, social and fatigue subscales

Table 1. Some recent clinical trials that have included QOL as an outcome

The aggressiveness of treatments in advanced ovarian cancer patients place more attention upon their QOL than patients diagnosed at an early stage. Several randomized clinical trials have been conducted in the first-line treatment of ovarian cancer. Clinical trials focus in important issues concerning the combination of surgery and chemotherapy, the identification of new targeted therapeutics and the route and timing of chemotherapy administration [48]. Paclitaxel in combination with a platinum compound is considered a

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standard care as first-line chemotherapy for advanced ovarian cancer. However, paclitaxel is associated with several toxicities (e.g. anemia, thrombocytopenia) that overlap the toxicities of the plantinums, and the co-administration of paclitaxel and a platinum compound can potentially increase the frequency and/or severity of shared toxicities. By itself, paclitaxel is associated with peripheral neuropathy that can add to the disease burden of the patient [4]. Therefore, studies have been conducted to find the least toxic combination of medications used in chemotherapy in order to improve treatment tolerability and QOL [49]. For example, a Phase III Trial conducted by the Scotish Gynaecological Cancer Trials Group (SCOTROC Trial), which included 1077 patients, compared carboplatin docetaxel with carboplatin paclitaxel for first line therapy. Results demonstrated a clear advantage for docetaxel in terms of neurotoxicity [43]. Concurrent with the developments in intravenous treatment, intraperitoneal treatment has also been shown a valuable strategy. The Gynecologic Oncology Group published data from the GOG randomized phase III trial (GOG 172) pertaining QOL outcomes associated with the use of intravenous paclitaxel plus intraperitoneal cisplatin plus paclitaxel, versus intravenous paclitaxel plus cisplatin, for advanced stage cancer [42]. This was the first Phase III GOG ovarian cancer that proposed a change in route for the administration of front-line chemotherapy. In the intraperitoneal arm, overall survival was improved by approximately 16 months; however, during active treatment, patients reported more QOL disruptions, abdominal discomfort and neurotoxicity compared to those patients receiving conventional intravenous chemotherapy. However, only neurotoxicity remained significantly higher for patients in the intraperitoneal arm 12 months post-treatment. Future studies to lessen the added burden associated with intraperitoneal therapy are going [42]. Recently, Vergote et al. [44] reported the results of a Gynaecologic Cancer Intergroup Collaboration Trial which compared upfront debulking followed by chemotherapy to neoadjuvant chemotherapy. This was the first randomized Phase III Trial of neoadjuvant chemotherapy in ovarian cancer using QOL as an endpoint. The two groups reported similar survival outcomes. QOL scores did not differ among the two groups [44].

The majority of ovarian cancer patients will eventually relapse. In fact, it is not uncommon for ovarian cancer patients to undergo numerous chemotherapeutics treatments. In this context, the evaluation of QOL is of utmost importance. In the management of recurrent ovarian cancer, tumour control without compromising QOL should be the goal of the therapy [50]. However, there are deficits in the measurement of general QOL data in the recurrent setting, in terms of QOL disruptions and number of studies including QOL measurements [26]. A recent trial published data pertaining the impact of early versus delayed treatment of recurrent ovarian cancer based on Ca125 measurements exceeding twice the upper limit of normal. Results showed that women did not live longer if chemotherapy was initiated earlier based on Ca125, as opposed to delaying treatment until symptoms developed. In addition, QOL was higher in women who underwent treatment at the time of clinical recurrence [47]. Despite the limitations of this study, these findings may have potential impact on clinical practice.

4.2. QOL in ovarian cancer survivors

Despite the considerable increase in the number of QOL studies carried out in ovarian cancer patients, few studies have focused, particularly, in assessing QOL in ovarian cancer survivors. Although, ovarian cancer patients do not belong to the most prevalent survivor population due to the aggressiveness of the disease and relatively low survival rates, it is of utmost importance to understand the QOL of those women who live years after the diagnosis without symptoms of the disease [9, 51, 52]. QOL has been evaluated namely among small samples of survivors by using mostly the EORTC QOL-C30, EORTC QOL-OV28 and supplemented by several other questionnaires to assess specific dimensions of QOL.

Overall, with the exception of the study conducted by Liaavaaq et al [53], available data suggests that ovarian cancer survivors have generally good QOL; however, specific deficits are reported and these are more prevalent in ovarian cancer survivors that in women without a history of cancer [52, 54-57]. Results concerning psychological functioning are inconsistent, ranging from good emotional status to psychological distress, including PTSD and depression. Below are described with more detail findings from recent studies examining QOL in ovarian cancer survivors.

Results from the study conducted by Steward et al [54] support the view that this group of survivors experiences overall good QOL. These investigators assessed 200 ovarian cancer survivors, who were at the time of the study without active disease and not on treatment, on physical, psychological and social well-being. On average, women had been diagnosed with ovarian cancer in the previous 7 years. Results showed that the majority of the survivors (89%) regarded their health as good or excellent. Participants also reported a better mental health and equivalent energy levels comparing to the general population. However, the majority of the women suffered from pelvic pain and discomfort (54%). Study findings also demonstrated that although 57% of the survivors referred that their sexual life had been negatively affected by the cancer and its treatment, their general sense of loss regarding sexual functioning was perceived as moderate to low. Unsurprisingly, women under 55 years of age reported a greater sense of loss about sexual functioning and fertility. According to these authors, the experience of surviving ovarian cancer appeared to have enriched these women, altering their life priorities and developing on them an impressive resilience [54]. Furthermore, authors highlighted that these survivors showed in general a great pleasure in life and relationships [54]. Similar findings were obtained in the study conducted by Wenzel et al [55], who examined 49 early stage ovarian cancer survivors (> 5 years). Findings revealed that survivors enjoyed a good QOL, with physical, emotional and social well-being comparable to other survivors and same aged samples without a history of cancer. Few deficits were reported, such as problems related to abdominal and gynaecological symptoms, and neurotoxicity. In the emotional domain, scores were more variable, with only one third of the survivors experiencing an excellent emotional well-being. Fears of future diagnostic tests (30%) and recurrence (20%) were also found. Investigators emphasised the resilience and growth that survivors reported in their study as a result of their ovarian cancer experience [55]. Another attempt to understand QOL in ovarian cancer survivors was carried out by Matulonis et al [56], who evaluated 55 early stage survivors. Findings demonstrated that

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survivors had good physical QOL, with few long-term physical symptoms (such as abdominal complaints and neurotoxicity) and few unmet needs. However, survivors reported emotional problems, such as psychological distress (40%), anxiety about Ca125 testing (54%), fear of recurrence (56%) and 26% had scores suggestive of PTSD. Better mental health was associated with less fatigue and pain, fewer stressful life events and higher social support. The authors reported as well sexual problems, namely pain during sexual intercourse (52%). Less than 10% of participants were interested in sex or were sexually active. Additionally, it was noted that younger survivors presented greater sexual problems. Similarly, Mirabeau-Beale et al [57] who conducted the first comparison between early stage (58 women) and advanced stage (42 women) survivors on QOL (> 3 years), physical, sexual and mental function, reported that survivors experienced positive overall QOL and long-term adjustment. Investigators reported no differences between early stage and advanced stage survivors on overall QOL, unmet needs, social support, complementary therapy use, physical symptoms (neurotoxicity, fatigue and comorbidities), functioning (cognitive, sexual, physical, role, emotional and sexuality), spirituality, hopelessness and psychological state. However, advanced stage survivors experienced better social functioning. Although, the majority of survivors had a good emotional functioning, scores suggestive of PTSD were noted in 7% of early stage survivors. Diagnosable PTSD scores were not found in the advance stage survivors group. Decreased sexual interest attributed to cancer, physical comorbidities, such as degenerative joint disease, gastrointestinal distress and thyroid disease, fear of recurrence, use of complementary and alternative medicines (exercise, vitamins, prayer and massage) in order to improve their QOL were reported by survivors. The most recent account on QOL in ovarian cancer survivors was given by Greimel et al [52], who attempted to fill a gap in the literature by conducting a prospective study on QOL in long-term survivors (> 10 years). This longitudinal study examined survivors at three time points: pre-treatment (baseline), 1-year after diagnosis and 10 years post-treatment using the EORTC QOL-C30. At the baseline, 33 survivors were included; of those, 22 died within 5 years post diagnosis and 11 survived beyond 10 years. In general, results corroborated previous findings reporting that survivors experienced a good physical, psychological, social and spiritual health. Despite no differences at baseline in FIGO stage, residual tumour, performance status and treatment characteristics between short-term and long-term survivors, the latter group experienced better physical functioning, role functioning, cognitive functioning and less symptoms than short-term survivors. Higher levels of symptoms and intra operative ascites were also more prevalent in the short-term survivors group. One year after treatment, the majority of the QOL dimensions were comparable among the two groups; however, long-term survivors reported better global QOL but more insomnia. Emotional functioning and global QOL improved significantly from baseline to 1 year after diagnosis and remained relatively stable in the 10 year follow-up evaluation. Long-term survivors did not experience more sleeping problems 10 years after their diagnosis than women from a general population [52].

Contradicting the trend described above, Liaavaaq et al [53] evaluated 189 ovarian cancer survivors (> 18 months after primary treatment) and found that survivors experienced poorer QOL, had more chronic fatigue and mental morbidity, used more medication and health services when compared to age-adjusted controls from the general population.

Recent studies attempted to improve methodological deficits observed in previous research, for example, by using more standardized and validate measures to assess QOL in this cancer population. However, small sample sizes, heterogeneity of samples, timing of assessment are among the difficulties posed by current research, which make problematic to reach definite conclusions. Despite this, collectively, existing studies highlight important issues and concerns experienced by ovarian cancer survivors. Beyond the expected physical and sexual sequalaes of the illness and treatment, studies highlighted, particularly, psychological difficulties faced by survivors, which may adversely affect their psychological adjustment and well-being. Findings from survivorship research are paramount to provide critical information to guide the development and design of interventions to assist survivors at risk.

The care provided to the cancer patient does not cease when the treatment ends. Survivorship is now recognized as a phase in the cancer trajectory that requires special attention and ongoing specialized care. In 2006, the Institute of Medicine (IOM) published a report on cancer survivorship entitled: 'From cancer patient to cancer survivor: Lost in transition' [58], identifying unique concerns for cancer survivors, recommending the development of a survivorship plan to be developed at the end of treatment for all people treated for cancer of any type. Examples of requirements of the survivorship care plan as recommended by the IOM include, among others, information on possible late and long term effects of treatments and symptoms of such effects, information on the possible effects of cancer on marital/partner relationship, sexual functioning, work and parenting and the potential future need for psychosocial support, referrals to specific follow-up care providers (e.g. rehabilitation, psychology), support groups, and/or the patient's primary care provider.

5. QOL in ovarian cancer: The challenges

Definitely, one of the main challenges in QOL research is to translate and apply the findings obtained in research settings to clinical practice. In fact, in order to fully take advantage of all the benefits offered by QOL research, it is imperative that QOL research provides health care professionals with clinically relevant and interpretable information that can guide treatment decisions. However, routine use of QOL measures has been limited in clinical settings [6]. Challenges of using QOL data to inform clinical practice may include the use of somewhat arbitrary cutoff points or magnitude of change in QOL scores to determine when therapeutic change is needed [26]. To optimize treatment decisions for patients with ovarian cancer, it is paramount that health care professionals are familiar with differences between treatment regimens regarding toxicity, dosage and administration but also findings from QOL measurements [11].

From the research perspective, there is a need for standardized collection and reporting of QOL data from ovarian cancer patients, such as use of common instruments that demonstrate the most sensitivity to the study hypothesis and outcomes of interest, common data collection time points, minimum expectations for data analysis and publication reporting guidelines. These would allow comparative effectiveness research to be carried out [18]. Fur-

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ther larger and rigorous studies are needed to fully understand QOL issues in ovarian cancer patients. Longitudinal studies examining QOL across the different phases of ovarian cancer trajectory would give valuable insights into the QOL of these patients.

As new treatment regimens for ovarian cancer continue to be developed and investigated in the hope of improving survival of patients, it is paramount that QOL is regarded as one of the most important endpoints in clinical trials. However, this is not sufficient. It is as well important to routinely assess QOL disruptions in patients in clinical settings in order to screen and identify patients at risk. Therefore, efforts should also be targeted to the development of interventions to be used in women at need, to prevent or ameliorate the negative impact of the illness on QOL. The assessment of QOL in clinical settings also allows the identification of QOL needs throughout the cancer trajectory.

6. Conclusion

Ovarian cancer patients may experience QOL disruptions and a wide range of sequalae that do not dissipate with time and may persist for a long-term period. Measuring QOL in ovarian cancer patients during the illness trajectory is of utmost importance. This is of great value to develop and design interventions to assist ovarian cancer patients at need, and as well to assist in the therapeutic decision process.

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