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INVITED RESEARCH ARTICLE

Quality of life in ovarian cancer survivors

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Abstract

Ovarian cancer survivors may experience Quality of Life (QOL) disruptions due to the aggressiveness of the illness and its treatment. The present manuscript intends to review the most recent knowledge regarding QOL in ovarian cancer survivors. Firstly, a brief overview about QOL, their importance and instruments used to assess it particularly in ovarian cancer survivors are presented. Then, main findings and developments achieved to date are discussed. Main conclusions from studies reviewed and future research needs are outlined. Available literature suggests that in general ovarian cancer survivors experience a good QOL; however, some deficits are more prevalent than in women without cancer. Although, these studies brought to light important QOL issues, more rigorous and larger studies are necessary to fully understand ovarian cancer survivors' QOL. Measuring QOL in ovarian cancer survivors in clinical settings is of utmost importance to identify those survivors at risk and provide adequate support that meets their needs.

Keywords: Quality of Life, Ovarian cancer survivors.

Introduction

Ovarian cancer is the most fatal malignancy of the female genital tract and the fourth most common cause of female cancer death (Siegel, Naishadham and Jemal, 2012). It is an aggressive illness associated with very poor survival and high recurrence rates. Generally, ovarian cancer is detected at an advance stage, with a 5-year survival rate of 46 % for all the stages and 31 % for advanced stages (Siegel et al., 2012). The management of ovarian cancer normally includes radical pelvic surgery and multiple aggressive courses of chemotherapy. Women may suffer debilitating disease-related symptoms, such as weight loss, bloating and ascites, fatigue and pain and a wide range of treatment sequelae (Gonçalves, 2010; Stavrika et al., 2012). Examples of treatment related sequelae 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 (Gonçalves, 2010; Stavrika et al., 2012).

The stress of receiving the diagnosis of such an aggressive and life threatening illness, may be associated with uncertainty and anxiety about the future. In fact, ovarian cancer may be perceived as a traumatic event and may have a strong psychological impact on the survivor and her Quality of Life (QOL) (Gonçalves, Jayson and Tarrier, 2008, 2011). Following this line, research carried out, specifically, with ovarian cancer patients has shown that a substantial proportion of women experience psychological disorders. Anxiety, depression and Post Traumatic Stress Disorder (PTSD) have been reported (Gonçalves et al., 2008; Huang, Cronin and Johnson, 2008; Gonçalves et al., 2011; Hess

and Stehman, 2012). Qualitative studies and Quality of Life studies have shown that significant distress, impairments in physical, vocational, social, familial and sexual functioning may also occur (WHOQOL, 1993; Bowling 2001; Ferrell et al., 2003; Norton et al., 2004; Gonçalves et al., 2011; Chase and Wenzel, 2011). In this context, we conducted a prospective longitudinal study to measure psychological disorders, such as anxiety and depression, perceived social support, neuroticism and coping strategies to control unwanted thoughts in ovarian cancer patients (Gonçalves et al., 2008). These were measured at similar time points; which were the beginning of chemotherapy treatment, mid-treatment, end of treatment and 3 months follow-up post-treatment. The results showed that there were three patterns of anxiety and depression over time: absence of caseness (never a case), occasional or intermittent cases and persistent cases (cases at all the time points). The majority of the women were cases of anxiety at some occasions (52 %), while 38 % were cases of depression at some time points. Also, a subset of women were persistent cases of anxiety (22 %) and a smaller number suffered persistent depression (6 %) (Gonçalves et al., 2008).

Although ovarian cancer patients do not belong to the largest cancer survivor population, there is a subset of women, who live years after the diagnosis without symptoms of the disease. Although, most of these survivors return to their normal functioning, they often need to deal with physical and psychological sequelae that persist for a long-term period and have a negative impact on their QOL. The understanding that the study of QOL outcomes in ovarian cancer survivors is of utmost importance, led to the emergence of a body of research that has been targeting QOL issues in ovarian cancer. The knowledge about these issues is crucial to provide appropriate clinical support that meets survivors' needs, and ultimately, improve their QOL. The present manuscript addresses the most recent knowledge regarding QOL in ovarian cancer survivors. Firstly, a brief overview about QOL, their importance and instruments used to assess it particularly in ovarian cancer survivors are presented. Then, main findings and developments achieved to date are discussed. Main conclusions from studies reviewed and future research needs are outlined.

Quality of Life: an overview

Although the definition of QOL is not consensual, it is generally accepted that it is a multidimensional construct that encompasses several important dimensions (any area of behavior or experience) (Cella et al., 1993; Ferrell et al., 2003; Gonçalves et al., 2008; Hess and Stehman, 2012). These include 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 (Ferrell et al., 2003; Hess and Stehman, 2012). According to the WHO (WHOQOL, 1993), 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". Therefore, QOL includes all aspects of the individual well-being and must be evaluated from the individual's perspective.

The study of QOL outcomes is very relevant in the context of health care provision. Primarily, QOL measurement provides information essential to guide clinical decision making (Higginson, 2001). 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 (Penson, Wenzel, Vergote and Cella, 2006). 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 (Jacobsen, Davis and Cella, 2002). In addition, it can help to shape public policy and health care decisions made by governmental and private institutions (Murphy, Ridner, Wells and Dietrich, 2007) and allow the economic evaluation of healthcare provision (Velikova, Stark and Selby, 1999).

In general, QOL assessment in ovarian cancer patients has been focusing more on the acute phase of the treatment. Researchers have been interested in 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. In fact, screening and early detection of ovarian cancer are very limited in clinical practice, existing narrow useful technologies to assist in early diagnosis. Regarding survivorship, recently, there is a growing interest in the study of QOL in ovarian cancer survivors; however, there are still few studies about QOL in this phase of the cancer trajectory.

Different instrument's measures have been developed to evaluate QOL in oncology settings. The most commonly used measures to assess QOL in ovarian cancer survivors are EORTC QOL-C30 and EORTC QOL-OV28, which may be supplemented by several other questionnaires to assess specific dimensions of QOL. The EORTC QOL-C30 is a cancer-specific questionnaire 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 (Aaronson et al., 1993; Cull et al., 2001). 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 quality of life, 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 items), 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 physical condition. The EORTC QOL-C30 has established reliability and validity (Aaronson et al., 1993). 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) (Cull et al., 2001; Greimel et al., 2003). The EORTC QOL-OV28 is a valid and reliable measure to be used in ovarian cancer populations (Greimel et al., 2003). These instruments have been developed primarily from research environments; however, they are extremely helpful if they assist physicians in detecting clinically significant differences or changes in a patient condition.

Quality of Life in Ovarian Cancer Survivors

Collectively, available literature suggests that ovarian cancer survivors have generally good QOL; however, specific deficits are more prevalent in ovarian cancer survivors than in women without a history of cancer (Steward et al., 2001; Wenzel et al., 2002; Matulonis et al., 2008; Mirabeau-Beale et al., 2009; Greimel et al., 2011; Teng, Kalloger; Brotto and McAlpine, 2014). An exception is made by a study conducted by Liavaag, Dørum, Fosså, Tropé and Dahl (2007) that found that ovarian cancer survivors were experiencing poorer QOL than healthy controls. Results concerning psychological functioning are inconsistent, ranging from good emotional status to psychological distress, including PTSD and depression (Liavaag et al., 2007). Findings from studies examining QOL in ovarian cancer survivors are described below.

One of the first studies addressing QOL in ovarian cancer survivors was conducted by Stewart, Wong, Duff, Melancon and Cheung (2001) on 200 ovarian cancer survivors, who were disease-free at the time of the study. They were assessed on physical, psychological and social well-being. Results showed that most of the survivors (89 %) regarded their health as good or excellent. A better mental health and equivalent energy levels comparing to the general population were found. However, the majority of the women experienced pelvic pain and discomfort (54 %). 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. Women under 55 years of age reported a greater sense of loss about sexual functioning and fertility. The experience of surviving ovarian cancer appeared to have enriched these women, altering their life priorities and developing on them an impressive resilience (Stewart et al., 2001). Furthermore, authors highlighted that these survivors showed in general a great pleasure in life and relationships (Stewart et al., 2001). Similarly, Wenzel and colleagues (2002), who examined 49 early stage ovarian cancer survivors (> 5 years), reported that survivors enjoyed a good QOL, with physical, emotional and social well-being comparable same aged samples without a history of cancer. Few difficulties 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 (Wenzel et al., 2002). Another study corroborated the view that ovarian cancer survivors experience a good QOL (Matulonis et al., 2008). Respondents experienced good physical QOL, 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. Sexual problems, namely pain during sexual intercourse (52 %) were also reported. Less than 10 % of participants were interested in sex or were sexually active (Matulonis et al., 2008). Similarly to previous findings, Mirabeau-Beale and colleagues (2009), 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, found that survivors experienced positive overall QOL and long-term adjustment. There were 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 advanced 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 (Mirabeau-Beale et al., 2009). A recent study conducted by Greimel and colleagues examined survivors at three time points: pre-treatment (baseline), 1-year after diagnosis and 10 years post-treatment. 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 tumor, 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. 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 (Greimel et al., 2011). Although the majority of studies have been reporting that ovarian cancer survivors experience good QOL, Liavaag and colleagues' study contradicted this trend. Authors found that 189 ovarian cancer survivors (> 18 months after primary treatment) experienced poorer QOL, had more chronic fatigue and mental morbidity, and used more medication and health services when compared to age-adjusted controls from the general population.

Quality of Life's needs of ovarian cancer survivors were investigated in a very recent pilot study conducted by Teng and colleagues (2014). A total of 102 ovarian cancer survivors completed the EORTC QOL-C30 and the EORTC QOL-OV28 questionnaires. Results shown that clinical factors, such as age, stage of the disease, histology did not

have a significant impact of survivors' QOL. Task completion, memory, concentration, anxiety and fatigue were the distress categories that were given the highest scores by survivors. Authors concluded that psychological factors have a larger impact on global QOL than physical symptoms.

Conclusion

Collectively, studies examining QOL outcomes in ovarian cancer survivors reported that survivors are generally able to enjoy a QOL, equivalent to their healthy controls; however, some deficits are more prevalent in ovarian cancer survivors than in women without a history of cancer. Beyond the expected physical and sexual sequelae of the illness and treatment, studies highlighted psychological difficulties faced by survivors, which may adversely affect their psychological adjustment and well-being.

Findings from survivorship research are of utmost importance 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. Over the years, there was a noticeable attempt to improve the methodological quality of studies, 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 assessments are among the difficulties posed by current research, which make problematic to reach definite conclusions.

Existing studies brought to light, important QOL needs of ovarian cancer survivors; however, further larger and rigorous studies are necessary to fully understand QOL in ovarian cancer survivors. Among others, these include the use of standardized measures and reporting of QOL data from ovarian cancer survivors and common data collection time points. These would allow comparative effectiveness research to be carried out (Hess and Stehman, 2012).

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. Furthermore, it is very important to routinely assess QOL disruptions in ovarian cancer survivors in order to screen and identify patients at risk. Therefore, efforts should target the development of interventions to be used in women at need, to prevent or ameliorate the negative impact of the illness and its treatment on QOL. The assessment of QOL in clinical settings allows the identification of QOL needs throughout the cancer trajectory, which includes survivorship.

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