Gynecologic Oncology xxx (2018) xxx–xxx

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

Quality of life, symptoms and care needs in patients with persistent or recurrent platinum-resistant ovarian cancer: An NRG Oncology/ Gynecologic Oncology Group study☆

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HIGHLIGHTS

- In recurrent ovarian cancer, the most common unmet need is in the symptom dimension.
- The most common symptom is fatigue.
- Nearing the end of life there are associations between symptoms, unmet need, and QOL.

ARTICLE INFO

Article history:
Received 10 March 2018
Received in revised form 8 May 2018
Accepted 9 May 2018
Available online xxxx

Keywords:
Quality of life
Symptoms

ABSTRACT

Objectives. The goals of treating recurrent platinum-resistant ovarian cancer are palliative, aimed at reducing symptoms and improving progression free survival. A prospective trial was conducted to determine the prevalence and severity of symptoms, and associated care needs.

Methods. Eligible women included those with persistent or recurrent platinum-resistant ovarian cancer with an estimated life expectancy of at least 6 months. The Needs at the End-of-Life Screening Tool (NEST), FACIT-Fatigue (FACIT-F), NCCN-FACT Ovarian Symptom Index [NFOSI-18]; Disease Related Symptoms (DRS), Treatment Side Effects (TSE), and Function/Well Being (F/WB) were collected at study entry, 3 and 6 months.

Results. We enrolled 102 evaluable patients. Initiation of Do Not Resuscitate (DNR) discussions increased over time from 28% at study entry to 37% at 6 months. At study entry, the most common disease-related symptoms

☆ This study was supported by National Cancer Institute grants to the Gynecologic Oncology Group (GOG) Administrative Office (CA 27469), the Gynecologic Oncology Group Statistical Office (CA 37517), NRG Oncology SDMC (1U10 CA180822) and NRG Operations (U10CA180868). The following Gynecologic Oncology Group member institutions participated in the primary treatment studies: University of Oklahoma Health Sciences Center, Women and Infants Hospital, Ohio State University Comprehensive Cancer Center, University of Virginia, Carolinas Medical Center/Levine Cancer Institute, Metro-Minnesota CCOP, University of California Medical Center at Irvine-Orange Campus, Wayne State University/Karmanos Cancer Institute, Froedtert and the Medical College of Wisconsin, Washington University School of Medicine, University of Wisconsin Hospital and Clinics, Baystate Medical Center, Cancer Research for the Ozarks NCORP, Mainline Health CCOP, University of New Mexico, University of Massachusetts Memorial Health Care, Case Western Reserve University, The Hospital of Central Connecticut, Evanston CCOP-NorthShore University Health System, Michigan Cancer Research Consortium Community Clinical Oncology Program, Northern Indiana Cancer Research Consortium, Northwestern University, University of Colorado Cancer Center – Anschutz Cancer Pavilion, Rush University Medical Center, State University of New York Downstate Medical Center, MD Anderson Cancer Center, University of Chicago and Wichita CCOP.

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https://doi.org/10.1016/j.ygyno.2018.05.017
0090-8258/

Care needs
Ovarian cancer

were fatigue (92%), worry (89%), and trouble sleeping (76%); 73% reported being "bothered by treatment side effects", which included nausea (41%) and hair loss (51%) neither of which changed over time. The most common NEST unmet needs were in the symptom dimension. The social dimension was associated with F/WB ($p = 0.002$) and FACIT-F ($p = 0.006$); symptoms were associated with DRS ($p = 0.04$), TSE ($p = 0.03$), and FACIT-F ($p = 0.04$); existential was not associated with any of the patient-reported symptoms; therapeutic was associated with F/WB ($p = 0.02$).

Conclusions. In patients nearing the end of life, there are significant associations between disease and treatment related symptoms and unmet patient needs, which do not change substantially over time. Careful exploration of specific end-of-life care needs can improve patient-centered care and QOL.

1. Introduction

Women with advanced ovarian cancer are living longer due to tumor reductive surgery, chemotherapy advances, new monoclonal antibodies, and multidisciplinary care [1]. Despite advances in clinical research, the majority of ovarian cancer patients diagnosed with advanced disease will eventually develop recurrence, become resistant to platinum agents and receive palliative treatment. Palliative care is specifically intended to improve the symptoms associated with terminal cancer. Such symptoms include physical, social, and psychological aspects of coping over the entire continuum of care [2]. Nevertheless, the relationships between the patient's unmet needs, disease, treatment-related symptoms, and quality of life (QOL) have not been well described for women with recurrent ovarian cancer.

Symptom management, the core of palliative care, is an integral part of cancer care throughout the course of disease. Gynecologic cancer symptoms are multi-factorial in character as the primary cancer frequently metastasizes to other abdominal organs [3]. Consequently, recurrent ovarian cancer patients may be on chemotherapy for prolonged periods of time [4], making it difficult to discern if symptoms are related to the disease or treatment side effects. Nevertheless, symptom management and disease monitoring require vigilance.

Patients with advanced incurable cancer have a diverse range of needs [5]. Although a number of advances have been made in the understanding and treatment of cancer-related symptoms and QOL these advances have not necessarily translated into an understanding of the full range of social, existential, and therapeutic needs [6]. Examples of unmet needs include financial hardship, struggles with relationships, and personal goals. Unveiling these issues in an ovarian cancer population remains unexplored.

The multidimensional trajectory of recurrent platinum resistant or refractory ovarian cancer patients has not been previously described [7]. This prospective observational study assessed the care needs, symptoms, and QOL in patients with platinum resistant or platinum refractory ovarian, fallopian and peritoneal cancers on chemotherapy and those not on active treatments. The purpose of this study was to identify significant symptoms and needs to establish optimal targets for future intervention research.

2. Methods

2.1. Patients

This study was approved by the Institutional Review Board of the participating hospitals. Eligible patients had persistent or recurrent epithelial ovarian, peritoneal or fallopian tube cancer that was platinum-resistant. Platinum-resistance was defined as <6 months from the date of the first platinum therapy to date of first evidence of recurrent or persistent disease per imaging, physical exam, or CA-125. Patients were eligible for the study whether or not they were receiving anticancer treatment. The patient's life expectancy was to be at least 6 months from date of enrollment, and the patient's consent was required.

2.2. Measures

Patient demographic and clinical data were obtained at study entry. Disease status, current cancer therapy, and performance status were collected at study entry, 3 and 6 months. Those patients on cancer therapy were evaluated for the presence of measurable disease at study entry using Response Evaluation Criteria in Solid Tumors' (RECIST) guidelines version 1.1 [8].

Patient-reported outcome measures (PROs) were collected at study entry, 3 and 6 months. Unmet needs were measured with the Needs at the End-of-Life Screening Tool (NEST). NEST is classified and aggregated into 4 dimensions, which include Social including: social Needs, Existential, Symptoms, and Therapeutic [9–11]. The tool consists of 13 questions: the social dimension includes financial, access to care, having someone close, and care-giving needs; the existential dimension includes distress, spirituality, settledness, and purpose; the symptom dimension includes physical and mental symptoms; the therapeutic dimension includes patient-clinical relationship, information, and goals of care. Each question evaluates the extent to which distinct needs are being met from the patient's perspective. Cut scores exist for each of the 13 needs with a score above cutoffs considered an unmet need. A domain score was also calculated using proration, if >50% of domain items were answered.

QOL was measured with the Functional Assessment of Cancer Therapy – Ovarian (FACT-O) [12]. Fatigue was measured with the FACIT-F (fatigue) subscale [13], neurotoxicity with the FACT/GOG-Ntx-4 subscale [14], and abdominal discomfort with the FACT/GOG-AD subscale [15]. Items were scored using a 5-point scale (0 = not at all; 1 = a little bit; 2 = somewhat; 3 = quite a bit; 4 = very much). According to the FACIT measurement system, a subscale score was the summation of the individual item scores if >50% of subscale items were answered. Negative statements (or questions) were reversed prior to score calculation. When unanswered items existed, a subscale score was prorated by multiplying the mean of the answered item scores by the number of items in the subscale. A total FACT-O score is the sum of the subscale scores if >80% of the FACT-O items provide valid answers.

Ovarian cancer symptoms were also evaluated with the NCCN-FACT Ovarian Symptom Index-18 (NFOSI-18), which includes subscales assessing disease-related symptoms-physical (DRS-P), disease-related symptoms-emotional (DRS-E), treatment side effects (TSE), and function/well-being (F/WB) which is designed specifically to measure symptoms in patients with advanced ovarian cancer. For negative statements (or questions), reversal was performed prior to score calculation. A higher score indicates better QOL/functioning or fewer symptoms/side effects for the FACT-O, the FACT/GOG-Ntx-4 subscale, the FACT/GOG-Ad subscale, the FACIT-Fatigue subscale, and NFOSI-18 subscales. DNR (Do Not Resuscitate) information was gathered during study entry, 3, and 6 months.

2.3. Statistical analysis

The prevalence and severity of patient-reported symptoms were measured with the NFOSI-18, defined as the percentage of patients

Please cite this article as: V.E. von Gruenigen, et al., Quality of life, symptoms and care needs in patients with persistent or recurrent platinum-resistant ovarian cancer: An NRG Oncolo..., Gynecol Oncol (2018), https://doi.org/10.1016/j.ygyno.2018.05.017