Gynecologic Oncology 137 (2015) 423–429

Contents lists available at ScienceDirect

Gynecologic Oncology

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

The sooner the better: Genetic testing following ovarian cancer diagnosis

E. Fox [a,b], J. McCuaig [b], R. Demsky [b], C. Shuman [a], D. Chitayat [a], M. Maganti [c], J. Murphy [b,d], B. Rosen [b,d], S. Ferguson [d], S. Randall Armel [b,*]

[a] The Hospital for Sick Children and University of Toronto, Toronto, ON, Canada
[b] Familial Breast and Ovarian Cancer Clinic, Princess Margaret Cancer Center, Toronto, ON, Canada
[c] Department of Biostatistics, Princess Margaret Cancer Center, Toronto, ON, Canada
[d] Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, University of Toronto, Toronto, ON, Canada

HIGHLIGHTS

- Examined when women with serous ovarian cancer prefer to be offered genetic testing
- The majority felt that the best time for genetic testing was at initial diagnosis.
- Family history of cancer was associated with a preference for earlier testing.

ARTICLE INFO

Article history:
Received 7 January 2015
Accepted 31 March 2015
Available online 11 April 2015

Keywords:
Serous ovarian cancer
BRCA1
BRCA2
Genetic testing
Genetic counseling

ABSTRACT

Objective. As treatment based genetic testing becomes a reality, it is important to assess the attitudes and preferences of women newly diagnosed with ovarian cancer regarding genetic testing. The objective of this study was to determine when women with a diagnosis of high grade serous ovarian cancer would prefer to undergo genetic testing and factors that influence this preference.

Methods. Women over 18 years of age with a known diagnosis of high grade serous ovarian cancer diagnosed between October 2010–2013 were identified via the Princess Margaret Cancer Center Registry. Participants completed a questionnaire, which obtained preferences and attitudes towards genetic testing, cancer history, and demographic information.

Results. 120 of the 355 women identified (33.8%) completed the questionnaires. The median age at time of ovarian cancer diagnosis was 57 years (range 35–84). The majority of participants in this study were offered (94.6%) and pursued (84.8%) genetic testing. In this cohort, testing was most frequently offered at diagnosis (41.8%) or during treatment (19.1%). In this study, women with high grade serous ovarian cancer felt that genetic testing should be offered before or at the time of diagnosis (67.8%). Having a family history of breast or ovarian cancer was significantly ($p = 0.012$) associated with preferring genetic testing at an earlier time point in the disease course.

Conclusions. Our results demonstrate that women with high grade serous ovarian cancer acknowledge the personal and clinical utility of genetic testing and support test implementation at the time of cancer diagnosis.

1. Introduction

An estimated 24,580 women are diagnosed with ovarian cancer in Canada and the United States each year [1,2]. Of these women, approximately 11 to 15% carry inherited mutations in BRCA1 and BRCA2 [3–6], higher than the mutation rate in breast cancer [7]. The discovery of the BRCA1 [8] and BRCA2 [9] genes has allowed for more accurate risk assessment and the implementation of screening and prevention programs [10]. However, despite this advance, many mutation carriers are not identified until after they develop cancer. Significant family history of breast or ovarian cancer is typically the impetus for pursuing genetic testing but studies have shown that 19–44% of women with ovarian cancer do not have a positive family history [6,11–13]. As such, many women who may harbor mutations are not being referred for genetic assessment and testing [14]. A recent study found that only 23% of women with serous ovarian cancer were seen for genetic counseling [14]. Of the women who had genetic testing, 31% were found to have a BRCA1 or BRCA2 mutation, 16% of whom had no contributory family history [14].

The decision to test for BRCA1 and BRCA2 mutations in women diagnosed with serous ovarian cancer can have implications for both the

* Corresponding author at: Familial Breast and Ovarian Cancer Clinic Main floor, Rm 704, 610 University Avenue, Princess Margaret Cancer Center, Toronto, ON M5G 2M9, Canada. Tel.: +1 416 946 2270; fax: +1 416 946 6528.
E-mail address: Susan.Randall@uhn.ca (S. Randall Armel).

http://dx.doi.org/10.1016/j.ygyno.2015.03.057
0090-8258/

patient and her family members. DNA testing for hereditary breast and ovarian cancer is currently used to guide risk management decision making [15,16]. Women with a positive test result have an increased risk of developing hereditary breast cancer, which is relevant in terms of breast cancer screening or prophylactic surgery once treatment is complete for ovarian cancer. Women who are found not to have a mutation in BRCA1 or BRCA2 can avoid high risk screening as well as breast cancer prevention which often includes mastectomy. In addition, the survival rate of BRCA1 and BRCA2 mutations carriers is higher than for women with sporadic ovarian cancer [17–19]. Detecting an inherited mutation also has implications for the patient's family. Identification of a mutation in an unaffected relative can allow for an individualized medical plan including high risk cancer screening and risk reduction strategies [20]. Currently, DNA testing for hereditary breast and ovarian cancer can be used to guide decision making regarding risk management [15]. As treatment options broaden, it is expected that more women will be referred for testing. For example, BRCA-associated ovarian cancer tumors have been found to respond better to platinum chemotherapy [4,16,21]. Studies have suggested that Poly (ADP)-ribose polymerase (PARP) inhibitors are highly effective in recurrent cancers among those with BRCA associated tumors [22,23]. A current clinical trial has shown improved progression-free survival using PARP inhibitors [24], and the FDA has recently approved its use as a treatment for advanced ovarian cancer patients with BRCA mutations [25]. As these examples illustrate, the ability to target therapies to the specific mutations is becoming a reality. Before these become widely incorporated into clinical practice, it is important to assess the attitudes and preferences of women newly diagnosed with ovarian cancer regarding genetic testing. Understanding when women with a new diagnosis of serous ovarian cancer would prefer to be seen for genetic counseling and genetic testing can help inform standardized guidelines to ensure that all eligible are referred at an appropriate time.

Previous studies have examined the perceived risks and benefits of genetic testing at the time of diagnosis of ovarian cancer. Understandably, 50% of women diagnosed with cancer experience high levels of depression and anxiety [26,27]. There is concern that adding the decision to undergo genetic testing at this time could increase distress in these patients. Although limited, the literature suggests that women diagnosed with ovarian cancer are willing to receive genetic testing of BRCA1 and BRCA2 at the time of diagnosis despite it being a time of high stress [7,15]. A recent study examining women's timing preferences found a lack of consensus over the optimal time for referral to genetic counseling [28].

Currently in Ontario, all women with a diagnosis of invasive serous carcinoma of the ovary, fallopian tube or peritoneum are eligible for genetic testing of BRCA1 and BRCA2 irrespective of family history. Despite their eligibility and the potential benefit the results may have on treatment, no consensus exists among physicians regarding when to refer women with a new diagnosis of invasive serous ovarian cancer for genetic testing.

In this study we examined when, during the course of their treatment, women with invasive serous ovarian cancer would prefer to have genetic testing as well as what factors influence this decision. Understanding the preferences of the target population and identifying potential barriers will help inform best practices regarding implementation of genetic testing for women with serous ovarian cancer.

2. Methods

2.1. Study population

This study received research ethics board approval from Princess Margaret Cancer Centre (PMCC) and the University of Toronto in Toronto, Canada. A list of patients diagnosed with invasive serous ovarian cancer from October 2010 to October 2013 at PMCC was identified through the PMCC Registry. In addition, gynecologic oncology clinic lists from PMCC were reviewed during April and May 2014 to identify patients with a diagnosis of serous ovarian cancer.

2.2. Procedures

This study was a cross-sectional observational cohort study and was conducted using a quantitative questionnaire based approach. A previously validated questionnaire addressing topics relevant to our study objective was not identified. The body of qualitative literature on the subject matter was reviewed to inform areas of questioning regarding timing preference for genetic testing. A questionnaire including demographic information, personal cancer history, family cancer history and preferences and attitudes towards genetic testing was created (Appendix 1). Questionnaires were distributed by mail (February to April 2014) or in clinic (April to May 2014) to patients with confirmed invasive high grade serous ovarian cancer. A total of 284 questionnaires were mailed out and 71 patients were approached in clinic, some of whom had received but not yet completed the mailed questionnaire.

2.3. Data analysis

Patient demographics were summarized using descriptive statistics. Data on continuous variables were reported as median and range, while data on categorical variables was reported as percentages and frequencies. Categorical variables were analyzed using Chi-Square or Fisher's exact test where appropriate. Continuous variables were analyzed using analysis of variance techniques. Statistical significance was chosen as $p\text{-value} < 0.05$. SAS V9.3 was used in all statistical analysis.

3. Results

3.1. Patient population

Sixty-three mailed questionnaires were returned for a response rate of 21%. In addition, the study was introduced to 71 patients in clinic and 59 questionnaires were returned for a clinic response rate of 83%. In total 122 questionnaires were returned with an overall response rate of 34%. Ten questionnaires were excluded from the analysis due to incomplete data or unclear responses and therefore the results from 112 participants are included in the analysis.

The relevant clinical and demographic data are summarized in Table 1. The majority of women who participated in the study were Caucasian (83.9%) and had completed some post secondary education (75.8%). The median age at time of completing the survey was 59 years (range 36–86) and the median age at ovarian cancer diagnosis was 57 (range, 35–84). Approximately half of the participants (55.4%) had a family history of breast or ovarian cancer. Participants were approached at varying points in their treatment for invasive serous ovarian cancer (Fig. 1). At the time of questionnaire completion, 16.1% (N = 18) were currently undergoing treatment for newly diagnosed invasive serous ovarian cancer, 50% (N = 56) had completed primary treatment, ranging from within 6 months to greater than a year from finishing treatment, and 23.3% (N = 26) were currently undergoing treatment for recurrence of their ovarian cancer.

3.2. Referral information

Women were asked if they were offered genetic testing of BRCA1and BRCA2 following their diagnosis of invasive serous ovarian cancer and whether they decided to pursue testing. 106 (94.6%) respondents reported being offered a referral for genetic testing, five (4.5%) had not been offered genetic testing and one (0.9%) was unsure if testing had been offered. Of the women who were offered testing, 89 (84.8%) reported having undergone genetic testing, four (3.8%) had a genetic counseling appointment pending, seven (6.6%) did not have genetic testing and five (4.8%) were uncertain if they had genetic testing.