Gynecologic Oncology 138 (2015) 109–114

Contents lists available at ScienceDirect

Gynecologic Oncology

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

Adherence patterns to National Comprehensive Cancer Network (NCCN) guidelines for referral to cancer genetic professionals

Terri Febbraro [a,*,1], Katina Robison [a,b], Jennifer Scalia Wilbur [a,b], Jessica Laprise [a,b], Amy Bregar [a], Vrishali Lopes [a,c], Robert Legare [a,b], Ashley Stuckey [a,b]

[a] Women and Infants, Warren Alpert Medical School of Brown University, Providence, RI, USA
[b] Program in Women's Oncology, USA
[c] Division of Research, USA

HIGHLIGHTS

- Genetic counseling and testing is being underutilized.
- Breast cancer patients are more likely to be referred for genetic counseling.
- Referred patients are likely to follow up with counseling and testing.

ARTICLE INFO

Article history:
Received 12 January 2015
Accepted 22 April 2015
Available online 28 April 2015

Keywords:
Hereditary cancer
Genetic counseling
Practice patterns

ABSTRACT

Objective. Genetic predisposition is responsible for 5–10% of breast cancer, 10% of ovarian cancer and 2–5% of uterine cancer. The study objective was to compare genetic counseling and testing referral rates among women with breast cancer that met NCCN referral guidelines to the referral rates among women with gynecologic cancers and determine predictors of referral.

Methods. Utilizing an institutional tumor registry database, patients from an academic women's oncology program were identified who met a subset of NCCN guidelines for genetic referral between 2004 and 2010. Patients diagnosed with ovarian cancer, breast cancer ≤50 years of age, or uterine cancer <50 years of age were included. A retrospective electronic chart review was conducted to evaluate for a genetic referral and uptake of genetic testing.

Results. 820 women were included (216 uterine, 314 breast, and 290 ovarian cancer). The overall genetic referral rate was 21.7%. 34% of eligible breast cancer patients were referred compared to 13.4% of uterine cancer and 14.5% of ovarian cancer patients ($p < 0.0001$). Younger age, breast cancer diagnosis, family history and earlier stage were all significant referral predictors. The odds of being referred increased with the number of affected family members. 70.8% of referred patients, consulted with genetics. Among those who consulted with genetics, 95.2% underwent testing.

Conclusions. Although increasing, genetic counseling remains underutilized across cancer diagnosis. Women with breast cancer are more likely to be referred than women with gynecologic cancers. Younger age, earlier stage and positive family history appear to be predictive of referral for genetic evaluation.

1. Introduction

Over the past two decades, with the completion of the human genome project, the ability to offer patients genetic testing to identify cancer predisposition has become an accessible and valuable tool in cancer risk assessments. Currently more than 100 genes have been identified that confer an increased risk of cancer [1] and over 50 hereditary cancer syndromes have been described [2]. More recently the introduction of next generation sequencing has reduced the cost and increased the efficiency of genetic testing while allowing for the assessment of gene panels [1].

Women harboring a deleterious BRCA 1 or 2 mutation have a 40–65% lifetime risk of developing breast cancer and a 11–40% risk of developing ovarian cancer [3]. Approximately 5–10% of breast cancer patients [4] and 13–16% [5–7] of ovarian cancer patients harbor a germline BRCA 1

* Corresponding author at: University of Chicago, Department of Obstetrics and Gynecology, Section of Gynecologic Oncology, MC 2050, 5841 South Maryland Avenue, Chicago, IL 60637, USA.
E-mail address: Terri.Febbraro@uchospitals.edu (T. Febbraro).
[1] Present address: University of Chicago, Department of Obstetrics and Gynecology, Division of Gynecologic Oncology, Chicago, IL, USA.

http://dx.doi.org/10.1016/j.ygyno.2015.04.029
0090-8258/

or 2 mutation. These rates are even higher in women with high-grade serous ovarian cancer and fallopian tube cancer [7,8].

Lynch syndrome, known for its contribution to hereditary colon cancer, is responsible for 10% of endometrial cancer in women younger than 50 years old, which often presents as the sentinel cancer [9]. The cumulative lifetime risk of endometrial cancer among women with Lynch syndrome is up to 71% [10,11]. In addition, women diagnosed with Lynch syndrome are at an increase risk for developing ovarian cancer compared to the general population (3–14% vs 1.4%) [11].

The National Comprehensive Cancer Network (NCCN), an alliance of leading cancer centers, has developed a comprehensive set of clinical practice guidelines to assist practitioners in the management of care for oncology patients. In 1998, guidelines to identify women at risk for hereditary breast and ovarian syndrome as well as Lynch syndrome were incorporated into the larger body of practice guidelines. These recommendations specify that any women diagnosed with epithelial ovarian/fallopian tube/primary peritoneal cancer, breast cancer diagnosed at or before the age of 50, or endometrial cancer diagnosed before the age of 50 should be referred for a genetic risk assessment [12,13].

Genetic counseling and testing offers a number of benefits, for both patients and their families. Genetic counseling assists women in making informed decisions about their health and treatment, improves knowledge of cancer genetics, modifies cancer risk perceptions, and reduces cancer associated anxiety [14,15]. BRCA mutation carriers may benefit from prophylactic surgery, utilization of chemoprevention, as well as increased surveillance. For example, risk-reducing salpingo-oophorectomy was associated with an 80% reduction in ovarian and fallopian tube cancer risk and a 50% reduction in breast cancer risk. Prophylactic mastectomy decreased breast cancer risk by 90–95% pending ovarian status [16,17]. In studies of women with BRCA1 or 2 mutations who underwent risk reduction salpingo-oophorectomy, occult gynecological carcinomas were identified in up to 9% of cases [18,19]. In addition, adherence to patient surveillance guidelines improves after genetic counseling and testing [20]. Family members of mutation carriers may have the opportunity to seek testing prior to the onset of disease and choose to take prophylactic actions.

Unfortunately, referral to genetic counseling is often low and has been reported to be lower among women with ovarian cancer compared to women with breast cancer [21]. Despite ovarian cancer being the most lethal of gynecologic malignancies, public awareness is much greater for breast cancer. Higher rates of breast cancer and greater media attention given to breast cancer may offer an explanation to this discrepancy.

The purpose of this study was to investigate genetic counseling referral rates for women with breast cancer compared to women with gynecologic cancers. Our secondary aim was to determine predictors of referral to genetic counseling.

2. Methods

An institutional tumor registry database was queried to identify women with breast carcinoma ("infiltrative ductal carcinoma", "infiltrative lobular carcinoma", "ductal carcinoma in situ", "lobular carcinoma in situ") epithelial ovarian/fallopian tube/primary peritoneal carcinoma ("serous carcinoma", "clear cell carcinoma", "endometrioid carcinoma", "mucinous adenocarcinoma") and endometrial carcinoma ("endometrioid carcinoma", "papillary serous carcinoma", "mixed cell adenocarcinoma", "clear cell carcinoma", "carcinosarcoma", "leiomyosarcoma", "endometrial stroma sarcoma") treated at The Program in Women's Oncology, Women and Infants Hospital, Brown University from 2004 to 2010. From this sample, eligible women were selected who met designated National Comprehensive Cancer Network (NCCN) hereditary breast and ovarian cancer and Lynch syndrome guidelines for referral to genetics. The eligibility criteria for inclusion included: a personal endometrial cancer diagnosis less than 50 years of age, breast cancer diagnosis at or before 50 years of age, or a personal history of epithelial ovarian, fallopian tube, or primary peritoneal cancer at any age [12,13]. Women with synchronous or metachronous primaries meeting the respective age inclusion criteria, were analyzed under both cancer diagnoses as each new diagnoses represented a trigger for referral. Women excluded from this study were known mutation carriers or had already undergone genetic counseling and testing prior to the first encounter at our institution, lacked documentation of follow-up provider encounters at our institution besides operative or pathology reports in the electronic medical record, cancer diagnosis outside of the study age criteria, women less than 18 years of age, and women with non-epithelial ovarian cancer histology. This project was approved by the hospital Institutional Review Board (IRB).

We conducted a retrospective electronic chart review of women meeting the inclusion criteria. All notes, which included letters from tumor board, office notes, inpatient progress notes and consultation notes were reviewed to assess for documentation of referral to cancer genetics. A patient was considered "referred for genetic counseling" if a discussion was documented between the physician and patient discussing referral or if a consultation note was generated from a genetic counselor. A patient was considered referred but not counseled if the conversation was documented between the physician and the patient however no consultation or genetic notes were found. Those patients who received genetic testing were identified by a positive or negative mutation test result noted in the electronic chart.

Data collected included: age at diagnosis, year of diagnosis, race, tumor histology and stage, treatment, documented family history, insurance type, treating provider, parity, Ashkenazi Jewish heritage, referral to genetics, timing of referral, acceptance of genetic testing and identification of a mutation.

Data analysis was performed with SAS version 9.2 (Cary, NC). Categorical variables were compared with chi-square of Fisher's exact test. Continuous variables were compared using ANOVA. An alpha level of 0.05 was used for statistically significance. Logistic regression was used to calculate odds ratio and 95% confidence intervals; 95% CIs for odds ratio excluding 1.0 were statistically significant.

3. Results

A total of 3032 women with breast cancer, 837 women with ovarian, fallopian tube or primary peritoneal cancer and 1689 women with endometrial cancer received treatment at Women and Infants Hospital between 2004 and 2010. Among the total cancer cases, 216 women with uterine cancer (12.8%), 901 women with breast cancer (29.7%) and 622 women with ovarian cancer (74.3%) were found to meet the inclusion criteria for this study. Based on a priori power calculation, to detect a 15% genetic testing referral difference between cancer diagnosis groups, 422 breast cancer, 234 ovarian cancer and 117 endometrial cancer charts meeting criteria for referral for genetics were needed. An interim analysis demonstrated statistical significance of the study and data entry was terminated with 100% of the eligible uterine cases (216), 34.9% of the eligible breast cancer patients (314) and 46.6% of the eligible ovarian cancer patients (290) entered.

Table 1 demonstrates the distribution of the patients categorized by the cancer diagnosis. Women with both uterine and breast cancer were diagnosed at an earlier stage (stages 0–2) than women with ovarian cancer (stages 3–4) ($p < 0.001$). More than 85% of women in each group identified as Caucasian. A reported family history of cancer was seen in 48.6–60.7% of the patients included in this study, with breast cancer patients having the highest percentage (60.7%, $p = 0.03$).

The overall genetic referral rate was 21.7%. As depicted in Table 2, the rate of referral was highest for breast cancer (34.1%) while the referral rates for ovarian cancer and endometrial cancer were 14.5% and 13.4% respectively ($p < 0.001$). Among women referred, 77.6% of breast cancer patients, 62.1% of uterine cancer patients and 59.5% of ovarian cancer patients followed up for genetic counseling ($p < 0.05$). Overall, 70.8% of women referred for genetic counseling were compliant with