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A universal genetic testing initiative for patients with high-grade, non-mucinous epithelial ovarian cancer and the implications for cancer treatment☆

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HIGHLIGHTS

- <25% of ovarian cancer patients in the U.S. receive recommended genetics services.
- We increased the rates of genetic counseling and testing to over 85% in our clinic.
- Various interventions were used to increase rates of genetic counseling and testing.
- Physician-coordinated genetic testing of ovarian cancer patients is an option.
- Genetic testing results can impact ovarian cancer treatment options.

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ABSTRACT

Objective. Genetic counseling (GC) and germline genetic testing (GT) for *BRCA1* and *BRCA2* are considered standard of care for patients with high-grade, non-mucinous epithelial ovarian, fallopian tube, and primary peritoneal cancers (HGOC). We describe a universal genetic testing initiative to increase the rates of recommendation and acceptance of GC and GT to >80% for patients with HGOC at our institution.

Methods. Data from a consecutive cohort of patients seen in our gynecologic oncology clinics between 9/1/2012 and 8/31/2015 for evaluation of HGOC were retrospectively analyzed. Data were abstracted from the tumor registry, medical records, and research databases. Descriptive statistics were used to evaluate patient characteristics and GC, GT, and PARP inhibitor use. Various clinic interventions were developed, influenced by the Plan-Do-Study-Act cycle method, which included physician-coordinated GT, integrated GC, and assisted GC referrals.

Results. A cohort of 1636 patients presented to the gynecologic oncology clinics for evaluation of HGOC during our study period, and 1423 (87.0%) were recommended to have GC and GT. Of these, 1214 (85.3%) completed GT and 217 (17.9%) were found to have a *BRCA1* or *BRCA2* mutation. Among BRCA-positive patients, 167 had recurrent or progressive disease, and 56 of those received PARP inhibitor therapy.

Conclusions. The rates of GC and GT recommendation and completion among patients with HGOC at our institution exceeded 80% following the implementation of a universal genetic testing initiative. Universal genetic testing of patients with HGOC is one strategy to identify those who may benefit from PARP inhibitor therapy.

1. Introduction

Approximately 10–20% of high-grade, non-mucinous epithelial ovarian, fallopian tube, and primary peritoneal cancers (HGOC) are hereditary, primarily due to germline mutations in the *BRCA1* or *BRCA2* genes [1–3]. A mutation in *BRCA1* or *BRCA2* confers a 40–66% lifetime risk of breast cancer and a 13–46% lifetime risk of ovarian cancer

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in women [4]. Identification of a BRCA mutation has implications for the treatment of HGOC and the management of inherited cancer risks in patients and their families.

The National Comprehensive Cancer Network (NCCN) *BRCA1* and *BRCA2* genetic testing guidelines were revised in 2007 to state that all women with epithelial ovarian, fallopian tube, and primary peritoneal cancers meet criteria for genetic testing, regardless of their age at diagnosis or family history of cancer [5]. The same statement was later reflected in the consensus guidelines of several professional organizations [6–8]. Despite these recommendations, fewer than 25% of patients with HGOC in the United States are referred for genetic counseling and testing [9–11]. Studies have suggested that physician recommendation and referral patterns may influence patients' access to standard of care cancer genetics services [12–15].

In 2007, <12% of patients with invasive epithelial ovarian cancer seen in the gynecologic oncology clinics at our institution were referred for genetic counseling [16]. In 2013, as part of an institution-wide research program, we implemented a universal genetic testing initiative in our gynecologic oncology clinics. This initiative was implemented with the goal of ensuring that at least 80% of patients with HGOC received a recommendation for standard of care genetic counseling and testing for *BRCA1* and *BRCA2*. Here we describe our experience implementing the initiative, including the development and assessment of clinic interventions used to reach our goal.

2. Patients and methods

Approval for the initiation and conduct of the quality improvement project was obtained from The University of Texas MD Anderson Cancer Center's Quality Improvement Assessment Board. Subsequently, for this retrospective data analysis, MD Anderson Cancer Center Institutional Review Board approval was obtained with a waiver of informed consent.

This was a cohort study of female patients who initially presented to the gynecologic oncology clinics for evaluation of suspected or confirmed diagnosis of HGOC from September 1, 2012, through August 31, 2015. All patients were seen by a gynecologic oncologist or medical oncologist within the gynecologic oncology clinics located at our main campus and/or our regional clinic locations. Patients under 18 years of age and those with ovarian tumors other than HGOC were excluded from analysis.

Data were collected from the institutional tumor registry, electronic medical records, and departmental databases, and were stored in a password-protected REDCap database [17]. Data included clinical documentation between September 1, 2012 and August 31, 2016, allowing for capture of disease status, and uptake of genetic counseling, genetic testing, and Poly (ADP-Ribose) Polymerase inhibitor (PARPi) use, within at least one year from the date of initial presentation to the gynecologic oncology clinics. The quality improvement metrics captured included rates of recommendation for genetic counseling and genetic testing, rates of completion of genetic counseling, rates of completion of genetic testing, and the outcomes of genetic testing (positive, negative, or variant), as defined in Fig. 1. Retrospective data included: patient demographics, vital status, prior and current cancer diagnoses, cancer treatment (including the use of PARPi therapy), genetic testing methodology, genes analyzed, dates of genetic counseling and genetic testing, clinic interventions used to promote genetic counseling and testing, and documented reasons for lack of genetic counseling and/or genetic testing.

3. Universal genetic testing initiative methods

A working group of gynecologic oncology stakeholders, including physicians, genetic counselors, advanced practice providers, nurses, clinical managers, and physician trainees, was assembled in 2008 to study and improve the rates of genetic counseling and genetic testing referral. The Plan-Do-Study-Act (PDSA) cycle method guided the initial quality improvement project design, but due to changing genetic testing guidelines, limited staffing, and lack of funding to support the project, the initiative was not fully implemented [18]. An institution-wide research program was announced in 2012, launched in 2013, and allowed the universal genetic testing initiative to be fully implemented in our gynecologic oncology clinics.

The working group reviewed gynecologic oncology clinic practice patterns and identified barriers that affected patients' access to genetic counseling and genetic testing. Clinic interventions were developed with the intention of reducing or eliminating these barriers, targeting issues within the control of the working group members, and minimizing clinic workflow disruptions. A variety of clinic interventions were created

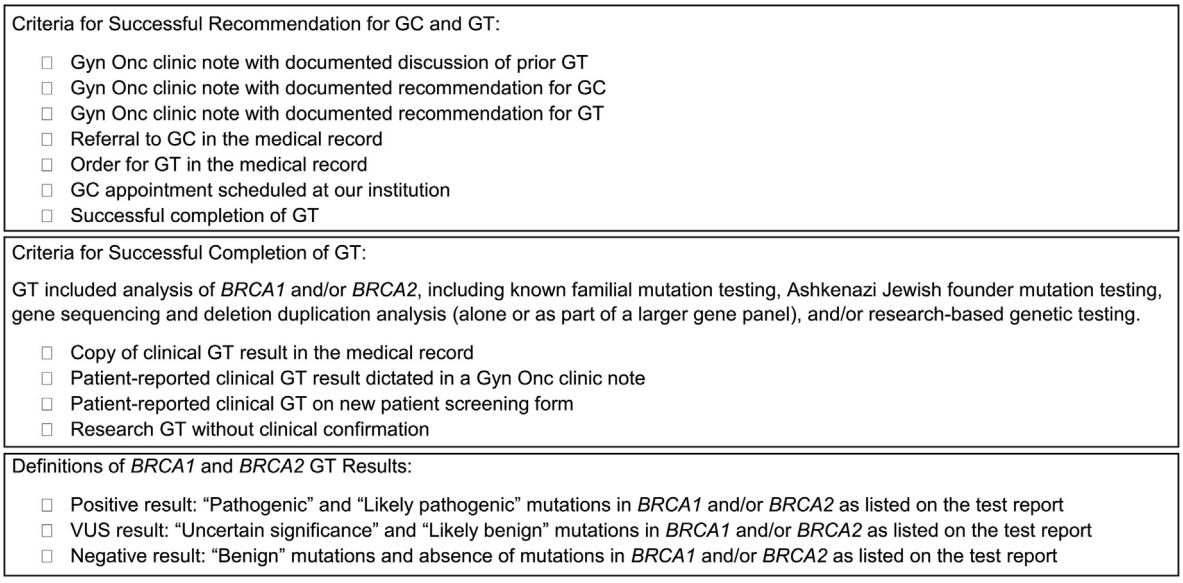

Fig. 1. Criteria for universal genetic testing metrics. For the task to be counted as "successfully completed," at least one item must have been completed in the category's check list. The criteria could be met prior to or following the patient's initial presentation to our institution's gynecologic oncology clinics. Genetic testing may have been coordinated by our institution or outside our institution. Abbreviations: GC, genetic counseling; GT, genetic testing; Gyn Onc, gynecologic oncology; VUS, variant of uncertain significance.

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