Evaluating the Uptake of Screening and Preventative Strategies for Patients at High Risk for Breast Cancer

Kala Visvanathan, MD MHS (JHU) and Monica Ter-Minassian, ScD (KPMAS)

Progress update 6/2018

Abstracts Presented: none

Background:

High-risk clinics have been in existence since the mid-1990s to late 1990s, however their impact in influencing preventive care for breast and ovarian cancer has not been well studied. With the increased accessibility of community- based and direct-to-consumer genetic testing, the expansion of genetic test offerings, there may need to be changes to the benefit and design of these multidisciplinary Clinical Genetics Services. At present some clinics see patients who test positive for a mutation or at high risk every few years once, others follow up every few years while others follow up the high risk patients every 6 months.

Current US guidelines recommend more intensive screening and preventive strategies for patients with a known pathogenic germline mutation or a high lifetime risk based on breast cancer risk prediction models. The American Cancer Society (ACS), for example, recommends that yearly mammogram alternating with MRI screening should be considered as early as 30 years old in women with a lifetime breast cancer risk of > 20%. Furthermore, risk reducing strategies for BRCA1/2 mutation carriers such (such as bilateral mastectomy, bilateral oophorectomy at age 35, or post child bearing and hormonal chemoprevention) have been recommended by NCCN [1][2].

1. Wuttke M, Phillips KA. Clinical management of women at high risk of breast cancer. Curr Opin Obstet Gynecol 2015; 27: 6-13.
2. Daly MB, Pilarski R, Axilbund JE et al. Genetic/familial high-risk assessment: breast and ovarian, version 1.2014. J Natl Compr Canc Netw 2014; 12: 1326-1338.

Objective:

Aim 1: Determine the incidence of preventive strategies post-initial clinical Genetics visit in women with and without cancer, with an identified BRCA1/BRCA2 mutation or strong family history of breast and ovarian cancer: 1) bilateral prophylactic oophorectomy and bilateral prophylactic mastectomy and 2) MRI/Mammogram screening

Aim 2: Preliminary study of changes in BMI, pre and post bilateral prophylactic oophorectomy in women at high risk for breast cancer, under 50 yrs old at time of surgery.

Aim 3: Determine the feasibility of extracting key covariates from the KP medical records for women identified to beat risk in Aim 1 to better define individual breast cancer risk. The covariates of interest include age of menarche, parity, age at first birth, benign biopsy, menopausal status, and number of 1st and 2nd degree relatives with cancer.
These variables are already available through self-reported questionnaires at JHU.

Methods: An 11 year retrospective review, between 2005-2016, accomplished using EMR data at KPMAS and an analytic population from the Breast and Ovarian Surveillance Service (BOSS)

cohort at JH. The Johns Hopkins Breast and Ovarian Surveillance Service Cohort study (BOSS) was an ongoing prospective study enrolling women (and men) with a familial risk for breast and ovarian cancer recruited from the cancer genetics clinic between 2005- 2013 with follow-up every 3 years to the present [3]. Patients completed a baseline questionnaire on characteristics such as demographics, weight, height, and cancer history. Pathology and treatment are confirmed in the medical record. At Kaiser Permanente Mid-Atlantic States, cases enrolled between 2005-2016 were identified with ICD diagnosis codes and utilization information extracted from the Research Data Warehouse (RDW) database. Patient characteristics on age, gender, race, weight, height and pregnancy history (parity), and benign biopsy extracted from the RDW, and CPT procedure codes used for surgical treatment and mammogram and MRI screening. In addition, sampled chart review was used to validate coded extractions and for extracting non- coded data. Patient characteristics between JHU and KPMAS will be compared by frequency counts and results merged. Given sufficient data, regression models will assess 1) significant covariates associated with the occurrence of prophylactic surgery and 2) significant covariates associated with screening completed every year post diagnosis and 3) significant covariates associated with changes in BMI, pre- and post-prophylactic oophorectomy.

3. Gross AL, May BJ, Axilbund JE et al. Weight change in breast cancer survivors compared to cancer-free women: a prospective study in women at familial risk of breast cancer. Cancer Epidemiol Biomarkers Prev 2015; 24: 1262-1269.

.

Results to Date:

Aim 1:

We found that 813 women that visited KP Genetics had a high risk for breast cancer diagnosis, with a median 51 yrs of age at dx, 45% White, 38% Black and 15% other race. Since genetics services for cancer were established recently, 98% of visits occurred after 1-1-2013.

500 patients were diagnosed with breast cancer (BC): 487 (60%) prior to the Genetics visit and 13 were diagnosed with BC post visit (6 over 180 days post visit). 331 patients had at least one mastectomy (found by diagnosis or procedure code), 230 prior to their visit, 101 post-visit (23 both pre and post visit). 27 patients received a prophylactic mastectomy (either 30 days prior to, or without, a BC diagnosis); 4 post Genetics visit.

51 women were diagnosed with ovarian cancer (OC), 49 prior to the Genetics visit, and 2 were diagnosed post visit. 132 patients received an oophorectomy (diagnosis or procedure code), 103 prior to the visit and 29 post visit. 91 patients received a prophylactic oophorectomy (without a diagnosis of OC), 27 post Genetics visit.

Of the 319 patients that had no prior breast cancer prior to, or within 180 days, of the Genetics visit, 181 (57%) had at least 1 screening mammogram or MRI post visit. 178 had one to three screening tests and only 3 women had four to six post Genetic screens during the study period. Almost all (180) patients that had at least one post Genetics screen, were screened between mid-2013-2016. 70% continued screening (mammogram or MRI) 12 months after dx, but only 30% were screened more than 18 months after dx.

We will compare to the BOSS cohort data, when the DUA is complete.

Aim 2: (Preliminary Analysis, mainly for quality control)

We found that 4271 women at KPMAS had an oophorectomy when they were 50 yrs old or younger (regardless of indication) with a high risk for breast cancer diagnosis between 2005-2016 (regardless of department). Oophorectomy type and indication have been abstracted and further restrictions will be applied. Median age at oophorectomy was 44 years old (12-50), and patients were 23% White, 48% Black and 29% other race. 30% were ever smokers. 46% had an

overweight/obese diagnosis and 15% had a diagnosis of diabetes. 634 (15%) received estrogen therapy, while 1518 (36%) received estrogen and progesterone hormone replacement therapy. Weight at study start was 82-414 lbs with 0.3% missing. Weight at oophorectomy ranged from 88 to 454 lbs with 6.6% missing. Weight 1 yr after oophorectomy was 85-467 lbs with 42% missing. Weight 2 yrs after oophorectomy was 91-467 lbs with 54% missing. Weight 5 yrs after oophorectomy was 81-417 lbs with 72% missing. Height at the study start and at oophorectomy were also abstracted and BMI changes pre and post oophorectomy will be evaluated after further QC and restrictions on indications.

Aim 3: Non-coded data have been abstracted from the KPMAS EMR for 30 cases. Data abstraction was used to verify *BRCA* gene mutation status and lifetime risk model predictions, menstrual status and oophorectomy surgical type.

Conclusions to Date:

Aim 1: Screening after a high-risk breast cancer appears to have limited frequency and duration. Long-term adherence should be emphasized. We are applying for an NCI grant to continue to examine long term follow-up in a larger cohort of patients that will include high-risk diagnoses from all departments (not restricted to Genetics) and examine bone-density screening as well. An abstract is planned for the San Antonio Breast Cancer conference in December.

Aim 2: Further analysis must be completed. Resources for data collection and analysis for a control group must be developed.

Aim 3: Case abstraction from the EMR was essential to verify key data elements.