Knowing your patients' cancer family history saves lives

The importance of cancer family history in everyday patient care

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With genomic technology advancing rapidly, we are quickly progressing into an exciting era where we will be able to practice truly personalized medicine and tailor patient care based on individual risk. To illustrate, every woman fits into one of 3 risk categories for breast cancer: those that carry sporadic, familial, or hereditary cancer risk. As the de facto primary care providers for many women, we have the responsibility to stratify every patient into one of these 3 categories in order to properly adapt screening and management decisions. Additionally, a focus on family history and risk stratification allows us the opportunity to detect those patients who carry one of several genetic mutations that dramatically increase their risk of developing cancer.

Cancer screening protocol depends on risk

Sporadic. This large subset of women, who have average, or sporadic, risk simply warrant general population screening with mammograms and have no need for additional testing. They should be discouraged from early "baseline" mammograms and other overly aggressive interventions which are not supported by evidence-based medicine.

Familial. This population of women can reduce their risk of breast cancer with earlier, more frequent, or intense, surveillance due to their family history of cancer, dense breast tissue, or other contributing factors. Women with elevated risk due to family history may benefit from breast magnetic resonance imaging (MRI) in addition to mammograms and breast ultrasound starting at least 10 years prior to the age of cancer diagnosis in the youngest affected relative.

Hereditary. A small subset of women carry the highest risk for a gynecologic cancer due to a hereditary cancer gene. BRCA gene carriers, for instance, should have their surveillance for breast cancer start 15 years earlier than average-risk individuals and may be offered oral contraceptive pills (OCPs) to decrease their risk of ovarian cancer. For these patients, surgical and reproductive options need to be discussed from an early age and their circle of care needs to include radiology, oncology, and reproductive endocrinology.

The bottom line. Family history guides many of our recommendations and should be viewed as a symptom of an underlying inherited condition.[1]

Disclosure
Dr. Ofer reports that he is a speaker for Myriad Genetic Laboratories.

IDENTIFYING YOUR PATIENTS AT HIGH RISK FOR CANCER

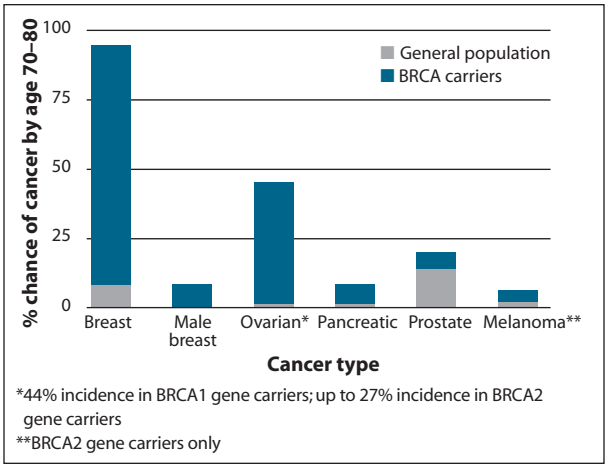
The family history questionnaire

Eventually, genetic screens may be done antenatally or at birth so that physicians can make the best decisions for each patient in regard to his or her screening, prevention, and overall care. We are at the edge of a genetics revolution; for the time being, however, with no such cost-effective, universal genetic screen available, there is one tool we currently have that provides us with valuable insight into our patients' genetic makeup: the family history questionnaire (FHQ). Taking a detailed family history costs almost nothing and takes a minimum amount of time for the clinician, yet it provides priceless information about each patient.

Hereditary gynecologic cancers: The extent of the nation and your practice

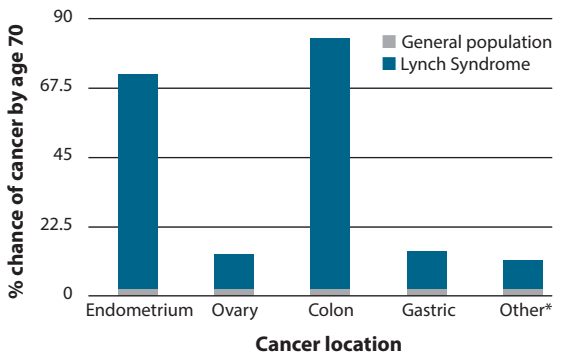
There are about 1 million people in the United States carrying genes for the most common hereditary gynecologic cancers: BRCA and Lynch syndrome (**FIGURE 1, FIGURE 2**).[2-7] Early diagnosis of their carrier status and interventions such as increased surveillance and prophylactic surgeries can dramatically reduce their risk of dying from cancers caused by their genetic mutations.[8,9] When physicians learn the red flags that indicate possible carrier status, implement a protocol that properly captures family history, and offer testing to appropriate patients,

FIGURE 1 Cancer incidence in BRCA carriers versus general population



*44% incidence in BRCA1 gene carriers; up to 27% incidence in BRCA2 gene carriers
**BRCA2 gene carriers only

FIGURE 2 Cancer incidence in Lynch Syndrome carriers versus general population



*Other cancers associated with Lynch Syndrome include hepatobiliary, ureteral/renal pelvis, small bowel, brain (usually glioblastoma), sebaceous carcinoma

we all come closer to saving those million women. To date, only about 10% of women with BRCA mutations, and only 1% to 2% of women with Lynch mutations, have been identified.[10]

Let's put these worrisome statistics in the context of what we gynecologists typically address as part of a routine well-care visit. During a patient's examination, most gynecologists feel it is important to perform a breast examination, pelvic examination, and Pap test. Pap tests help to diagnose approximately 12,000[11] cervical cancers per year; Pelvic examinations are a fairly ineffective screen for the approximately 20,000[12] annual cases of ovarian cancer in the United States;[12] and clinical breast examinations only catch approximately 3% of breast cancers that would not have been caught on a routine mammogram.[13] However, using something as simple as a FHQ and instituting a protocol to test appropriate patients can diagnose carrier status in most of the 1 million US women carrying a gene that significantly increases her mortality.

Considering the relatively common prevalence of hereditary cancer syndromes, such as BRCA and Lynch Syndrome, every average size Ob/Gyn practice must have a handful of patients who carry these mutations. Early diagnosis of these patients' genetic mutations not only affects the course of their disease but also the disease of countless relatives in current and future generations. Significant reductions in morbidity and mortality can be achieved through opportunities for early screening, prophylactic surgeries, and in vitro fertilization (IVF) with preimplantation genetics to eliminate the passing of this gene to future generations.

Unfortunately, use of a detailed FHQ and focus on such hereditary cancer risk assessment has been underutilized in clinical practice.[14]

BEYOND CANCER PREVENTION

Her family cancer history is important to her lifestyle choices

While 9% to 10% of patients in a typical primary care practice have risk factors that classify them as high risk for a gynecologic cancer based on their family history, most patients do not carry one of the known hereditary cancer mutations.[15] However, those patients still carry an elevated risk of cancer due to their family history and meet criteria for more intense surveillance than a patient at average risk for cancer. Family history is an important risk factor (independent of gene carrier status) in breast, colorectal, ovarian, and prostate cancers.[16] A woman with an affected first-degree relative is about twice as likely to develop breast cancer with the risk being higher when the relative was diagnosed before the age of 50 and when the number of affected relatives increases.[17]

Taking a moment to review with your patient her increased risk of cancer due to her family history is likely to have a substantial effect on her health. Women who perceive that their risk is elevated have been shown to be more compliant with annual mammography.[18] The addition of breast MRI to the screening algorithm can detect cancers as small as 1 mm to 2 mm and increase survival in women who do develop breast cancer.[19,20] Having a protocol in place to assess family history and discuss appropriate recommendations based specifically on that patient's risk has the ability to save more lives than many of the more invasive interventions we take in our practice.

Her family cancer history guides many of your patient management decisions

The following 4 cases highlight that in obstetrics and gynecology, our patients' cancer family history is important to almost every decision we make in the process of providing optimal care.

CASE 1 Optimal menorrhagia treatment in a potential Lynch syndrome carrier

Your 47-year-old patient has worsening menorrhagia. Results of her office endometrial biopsy and saline ultrasound are both normal. The patient expresses interest in having you perform an endometrial ablation procedure. Her FHQ shows that her brother had colon cancer, diagnosed at age 42, and an aunt had endometrial cancer at age 65.

Is it wise to go ahead with the endometrial ablation procedure?

Endometrial ablation may be a reasonable option for this patient; however, the option should not be considered until it is determined whether or not she is a Lynch syndrome carrier. This patient's brother had colon cancer younger than age 50, and he has a relative with another Lynch syndrome cancer (the aunt with endometrial cancer). Based on the brother's cancer history, he has a 27.5% chance of carrying a Lynch mutation. Your patient, his sister, has a 13.8% chance of carrying a Lynch mutation.[21]

For a Lynch mutation carrier, endometrial ablation would not be the optimal treatment for menorrhagia, as it may create uterine adhesions that may preclude adequate endometrial sampling in the future. A more optimal treatment recommendation for a carrier of a Lynch mutation, due to the risks of both endometrial and ovarian cancer, would be total hysterectomy with bilateral salpingo-oophorectomy (BSO). She also would need to see a gastroenterologist for yearly colonoscopies and close surveillance to decrease her risk of death from colon cancer.

CASE 2 Ideal contraception for a potential BRCA carrier

A 24-year-old nulliparous woman presents for contraceptive counseling. She is interested in a levonorgestrel-releasing intrauterine system (LNG-IUS). Her FHQ reveals that her mother had breast cancer at age 40 but is alive and well.

Is an LNG-IUS a good choice for this patient?

National Comprehensive Cancer Network (NCCN) criteria for hereditary cancer testing include having a first- or second-degree relative diagnosed with breast cancer younger than age 45. If this patient carries a BRCA gene mutation, OCPs would be a more appropriate contraceptive choice as they would address the menorrhagia as well as decrease the patient's risk of ovarian cancer. This patient will also need to start breast imaging with mammograms and MRIs by age 25 if she carries the gene and at age 30 if she does not.

CASE 3 Accurate preconception counseling for potential BRCA carrier

A 26-year-old nulliparous woman brings her husband with her to her annual well-care visit, as they will soon attempt pregnancy and want to discuss expectations and concerns with you. An FHQ is given to both the husband and wife to aid in preconceptual counseling. The husband's questionnaire reveals that his mother recently died of ovarian cancer at age 55.

Does the husband's family history of ovarian cancer affect your counseling at a preconceptual visit?

Any patient with ovarian cancer has a 10% to 12% chance of carrying a BRCA mutation.[22] In this case example, the patient's husband has a 5% to 6% chance of carrying a BRCA mutation. (His risk is 50% of his mother's.) If this couple becomes pregnant, their child will have a 2.5% to 3% chance of carrying the BRCA gene.

Testing the patient's husband for a BRCA mutation before conception can, and likely will, rule him out as a BRCA mutation carrier. If he does carry the gene, however, knowing this fact would allow you to refer him for proper cancer surveillance, help him to alert his other relatives who may be at increased risk for certain cancers, and allow your patient the opportunity to have IVF with preimplantation genetics to eliminate any chance that her child will receive this gene.

CASE 4 Appropriate fibroid management in potential BRCA carrier

A 42-year-old, P2 woman presents for a second opinion regarding treatment of multiple intramural fibroids causing pelvic pain and menorrhagia. Although she does not desire future fertility she has "done a lot of research" and strongly desires her uterus spared and a myomectomy to be performed. Her FHQ shows that she has two sisters who both had breast cancer in their late 40s, and her mother recently died in her 70s of breast cancer. The patient is not Jewish. She sees a breast surgeon twice per year for clinical breast examination and review of her mammography findings due to her family history.

Would a laparoscopic myomectomy be the appropriate procedure for this patient?

Whether you agree that a multiparous woman with no desire for fertility should have a myomectomy or not, you cannot treat this patient without knowing her carrier status for BRCA. Two women with breast cancer under age 50 in a family meets NCCN criteria for genetic testing. She has 3 family members with a history of breast cancer, 2 of which are younger than age 50.

This patient in my practice turned out to be a carrier of a BRCA1 mutation. The correct management recommendation was a hysterectomy with prophylactic BSO. Final pathology showed bilateral microscopic fallopian tube cancer, which is not an unusual finding in such a case. In fact, in BRCA1 carriers undergoing prophylactic BSO, microscopic tubal cancer can be found in as much as 17% of patients.[23] She has received 4.5 months of chemotherapy and her prognosis is excellent. Without genetic testing, her treatment, and likely her prognosis, would have been very different.

If this patient's genetic test results came back negative for the BRCA gene, we could have offered her ovarian conservation, as she had initially requested. However, she would still need to be treated very differently for her increased breast cancer risk. If her BRCA test was negative, Tyrer-Cuzick risk assessment would have shown that she still would have a 26% lifetime risk of developing breast cancer based on her family history. **(Free download for the Tyrer-Cuzick risk assessment tool is available at: http://www.ems-trials.org/riskevaluator.)** Based on that finding, she could be offered chemoprevention with tamoxifen, and she should undergo yearly breast MRI as well as mammography and breast ultrasound.

Either way—with the genetic test negative or positive for BRCA—the few minutes spent focusing on this patient's family history and reviewing her options for intervention likely will have a greater impact on her health than any other intervention I could have taken in the office, surgical or otherwise.

DEVELOP A PROTOCOL FOR ASSESSING FAMILY CANCER HISTORY

As we struggle to get through our busy office schedules and juggle the many demands on our time, how do we include a thorough gathering and assessment of family history without slowing down our practices? The answer is a protocol that once implemented and practiced will be effective and efficient.

An office protocol typically includes developing a FHQ that is handed to every patient at least once per year. In my office, the questionnaire is handed out after the patient returns the other routine paperwork (HIPPA forms, etc). They are told that their family history is very important in guiding the recommendations I will make, and they are allowed to hold on to the questionnaire until they are called back by the medical assistant. That gives patients as much time as possible to recall their family history.

My medical assistant then clarifies any questions with the patient and inputs the family history into the patient's electronic health record. The assistant also circles in red on the

hard copy FHQ any red flags that appear to be positive for a genetic mutation and leaves the FHQ at the top of the paperwork stack on the examination room door. When I walk into the examination room, it is always in my hand and on my mind.

Most patients (about 90%) have no significant family cancer history and the questionnaire has saved me time since the patient and my medical assistant already have spent the time gathering the information. About 1 in 10 patients has a significant finding, which must be reviewed and discussed. In appropriate patients, it only takes a few minutes to provide appropriate counseling regarding why they meet criteria for hereditary cancer testing, how it will impact their entire family's health management, and why even if the test result is negative they are likely to still be at high risk for cancer due to their family history. These tests are treated like any other important test we do in our office; patients are tested on the spot and every patient (negative, positive, and cancelled test) is instructed that they must come back for a follow-up visit.

I do not tell the patient that her follow-up visit is for the test "results." I explain that the results are most likely to come back negative for a genetic mutation, but that, because of her family history, it is very important to discuss her other relatives, who perhaps should be tested for hereditary cancer, and to outline a personalized cancer screening plan to minimize her familial risk of cancer. Those follow-up visits are reimbursed by insurance, increase patient satisfaction, and are a valuable tool in preventive medicine.[24]

ENCOURAGE YOUR PATIENTS TO COLLECT THEIR FAMILY MEDICAL HISTORY

In an incredibly high-tech world of medicine, it is almost surprising the positive impact we can make with a low-tech tool such as a FHQ. The first step is to recognize that family history is not just a minor obligation for our standard H&P; rather it is as important as any symptom our patients report.

Not only do we need to do our part in collection and review of our patients' family histories, we must encourage our patients to do their part as well. Almost all patients feel that family history is important in relation to their health, yet only 30% of those patients actively collect family health data.[25] Within our routine discussion of family cancer history with our patients, we need to encourage them to actively collect details of their family history. Holidays and other family gatherings can be a great time to share information among family.

THE STANDARD OF CARE IS UPON US

With our understanding of cancer genetics progressing rapidly, collecting a detailed family cancer history is quickly evolving to be a true standard of care. Physician practice tends to be slow to evolve. In this case, however, we cannot afford to take our time. Every day that we do not focus on family cancer history represents lives lost and our exposure to a growing medical–legal risk. Patients with cancer are being contacted by attorneys who are equipped with the recommendation by the American College of Obstetricians and Gynecologists that we take a detailed family cancer history and provide counseling about genetic testing to appropriate patients.

The lawyers have taken the time to learn NCCN guidelines, red flags for genetic testing, and surveillance options that should be recommended for high-risk women. It is time for every Ob/Gyn to do the same and to realize that family history plays a role in every management decision we make.

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