Veda N. Giri, MD

A NEW CHIEF AND NEW PLANS FOR CLINICAL CANCER GENETICS

Steve Kemper writer **Peter Baker** photographer

The field of genetic testing for cancer is rapidly evolving. Veda N. Giri, MD, the new Chief of the Division of Clinical Cancer Genetics at Smilow Cancer Hospital and Yale Cancer Center is at the evolution's forefront. The field's dynamism excites her, and she has ambitious plans for a novel, comprehensive program at Yale.

"I'm a medical oncologist by training," Dr. Giri said, "and I've always had a deep interest in treating patients and in cancer risk assessment. Cancer genetics marries those two interests. Genetic testing has become central for informing us about better strategies for treating patients who carry specific genetic mutations, tailored cancer screening, and hereditary cancer assessment for patients and their families."

Dr. Giri joined Yale from Thomas Jefferson University, where she was director of Cancer Risk Assessment and Clinical Cancer Genetics since 2014. While the field of genetic testing has been grounded in assessing hereditary cancer risk, the field of precision medicine has skyrocketed the volumes of patients needing genetic testing to inform cancer treatment. "Patients and providers are increasingly interested in thinking about what genetic tests should be done to inform decisions about cancer treatment," said Dr. Giri. For example, multiple PARP inhibitors have been approved for use in the treatment of patients with a variety of cancers who carry mutations in DNA repair genes, such as BRCA1 or BRCA2, due to clinical responses. As such, patients may be referred for genetic testing to inform cancer treatment, but it still requires that patients understand hereditary cancer risk, which can be uncovered by genetic results.

Genetic evaluation requires that patients receive information to make an informed decision for genetic testing. Since germline testing involves uncovering hereditary cancer risk, the first step, she continues, is explaining basic heredity to patients: we inherit half of our DNA from each parent, and our genomes carry more than 25,000 genes. Genetic testing assesses genes of interest based on the cancer of concern and can also uncover additional cancer risks. For instance, a man with prostate cancer—one of Dr. Giri's interests—may show a mutation in the BRCA2 gene, which signals risk not only for aggressive prostate cancer, but for pancreatic cancer, male breast cancer, and melanoma. Cancer risks for females with BRCA2 mutations include pancreatic cancer, female breast cancer, ovarian cancer, and melanoma. Since this is hereditary cancer testing, children have a fifty percent chance of inheriting mutations, and the associated cancer risks. "There is a ripple effect in families, since the genetic mutation should be tested in all blood relatives and inform tailored cancer screening," said Dr. Giri.

One key reason for genetic testing, she adds, is to inform cancer screening and prevention. If that man with prostate cancer passes on a BRCA2 mutation to his son, Dr. Giri would recommend that the son start screening for prostate cancer at age 40 instead of age 50, which is the recommendation for average-risk individuals. She also would discuss screening for pancreatic cancer especially if there is a family history of pancreatic cancer, and an annual clinical breast exam starting at age 35 for male breast cancer screening. If the patient's daughter inherits the mutation, likewise, Dr. Giri would discuss screening for pancreatic cancer, and instead of an annual mammogram starting at age 40, Dr. Giri would discuss breast cancer screening starting at age 30 or younger based on family history of breast cancer with the addition of breast MRI. For females, the national guidelines also recommend risk-reducing surgery to remove the ovaries around ages 40-45 or after childbearing due to the higher risk for ovarian cancer in females who carry BRCA2 mutations.

"The testing can be lifesaving, as far as identifying hereditary cancer syndromes. It really has a population-level impact."

Dr. Giri sees this intersection of genetic testing, clinical care, and population science as the future of cancer genetics. She has studied inequities in the availability of genetic testing for minority and underserved populations. To address the issue, she and her team developed projects to provide education on hereditary syndromes and the importance of genetic testing for individuals and their families.

One initiative recruited African American men and trained them as "peer genetic navigators" to educate individuals in their communities about prostate cancer and genetic testing. "The uptick of interest was remarkable," said Dr. Giri. When the rising volumes of patients in need of genetic testing led to a relative shortage of genetic counselors, Dr. Giri devised an inventive work-around: an educational video that patients with prostate cancer could watch to receive information about genetic testing. More than 70 percent of patients chose the video, and 94 percent of them proceeded to genetic testing. This was the first published patient-choice study of a pretest video in a male population regarding prostate cancer genetic testing.

"Thinking of novel strategies to deliver genetic information and access to genetic testing is very exciting to me," she said. "I plan to bring innovative models across cancer types so we can have an integrated effort to raise awareness across the diverse and underserved populations served by Yale, and ensure that standard-of-care genetics services are available across all clinical settings in the Smilow Cancer Network. That's one of my primary goals."

She also intends to leverage innovative genomic technologies to explore the genetic risk for cancer across diverse populations. These technologies can include expanded multigene testing, large-scale genomic testing, exome sequencing, and RNA testing to help clarify genetic contribution to cancer. She notes that about 80 percent of the studies on genetic markers for the risk of cancer are based on Caucasian populations, creating a gap in the data for diverse populations. "Let's investigate and see what genetic information we can find about cancer risk across diverse populations to ensure that genetic results are informative to cancer screening and treatment to each patient we see," she said.

"There are multiple areas that deserve expanded and deeper innovative strategies regarding genetic evaluation, cancer screening, and precision medicine to serve our patients and communities," she said. "From team-based approaches, we can make major strides to address gaps in genetics knowledge, explore family history, and expand access to genetic services. We can focus to engage with the community, reduce disparities and enhance equity regarding the benefit of genetic evaluation, and provide support for patients and their families."

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