Genetic predictions fail to pass the test

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By Shan Juan(China Daily)

Although genomic testing is making ground in China, many experts are warning that the procedures are flawed, and that patients are failing to act on the results. Shan Juan reports.

When Lily (not her real name) received the results of a genomic test she had taken, she was relieved and delighted to discover that it had ruled out the possibility of a higher-than-average risk of breast cancer.

The 30-year-old real estate agent in Guangzhou, Guangdong province, had feared she would develop the disease as a result of her fast-paced working life and hyperplasia, a precancerous condition that was discovered in her breast last year.

In early March, after her aunt was diagnosed with the disease, Lily signed up for a genomic test that was advertised as "predicting" breast cancer. She ordered a testing kit online, and when it arrived she carefully followed the instructions. She wiped the inside of her mouth with the oral swab sticks provided before mailing the samples to a consumer genetics lab in Guangzhou.

The Chinese literature major, who has a 2-year-old son, had never heard of genomic, or DNA, testing until 2013. She only became aware of it when news broke that the actress Angelina Jolie had undergone a double mastectomy and later had both ovaries removed because doctors had detected the presence of a "mutated" BRCA (breast cancer) gene. The faulty gene, which gave her an 80 percent chance of developing breast cancer and a 40 percent chance of ovarian cancer, had been detected via a genomic test, which identifies changes to chromosomes, proteins and genes.

**Public interest**

The news prompted widespread public interest in predictive genomic testing in China, and also provided opportunities for businesses that provide test kits to hype their products.

A click on any large e-commerce platform results in lists of home genetic-testing services that operate through the mail, with the cost ranging from several hundred to tens of thousands of yuan.

The companies claim that the tests can predict heart disease, most forms of cancer, diabetes, Alzheimer's disease and even obesity. They say the results can help to determine and deliver targeted prevention that, coupled with lifestyle changes, can save lives.

Predictive services test an individual's DNA for genetic variations that may raise the risk of developing certain diseases. They are intended to influence patients and prompt them to adjust their lifestyles to reduce the risks, according to the test companies.

However, those claims rarely stand up to scrutiny, according to a study conducted by researchers at the University of Cambridge in the UK, the results of which were published in the British Medical Journal last month.

The researchers concluded that although the tests can suggest a higher level of risk, they fail to prompt changes that could reduce those risks.

**Immature technology**

Zhong Nanshan, a respiratory expert and academic at the Chinese Academy of Engineering, said predictive genomic testing is an immature technology and not yet ready for wide promotion and application.

"For individuals, it's not worth doing, and it shouldn't be used so often to 'predict' diseases," he said.

However, he admitted that genomic testing is a good tool for early forecasting of certain inherited conditions such as Thalassemia - a disorder that can affect the amount of oxygen carried in the blood - and congenital deafness.

Chen Wanqing, director of the Chinese National Central Cancer Registry at the National Health and Family Planning Commission, said given that most illnesses involve the interaction of dozens, or even hundreds, of genes, coupled with an individual's environment and lifestyle, "this type of predictive genetic testing is mainly about business hype in most cases".

According to Chen, genomic testing, which is recognized by China's health authorities, is mainly used for the diagnosis and treatment of cancers, but accurately predicting the risk of cancer is difficult. The procedure also requires more research because little is known about the pathogenic genes of most cancers.

Ying Jianming, deputy director of the pathology department of the Cancer Institute and Hospital at the Chinese Academy of Medical Sciences, said doctors can gain better insight into potential illnesses by looking into the makeup of inherited genes that are faulty and therefore susceptible to mutation.

He cited Jolie as an example; her mother died from ovarian cancer, and the actress later discovered that she had inherited a faulty BRCA1 gene from her mother.

The presence of the gene - which regulates cell growth, but can increase the chances of cancer developing if it mutates - raised Jolie's risk of breast and ovarian cancer to 10 times higher than the average for women. Excision or removal of potentially affected organs or limbs can reduce the risk by 80 percent.

"So, she made her own medical choice (to have surgery), but it's one that can't be used widely because of the high cost," Ying said. He added that the risk of legal action further down the line means few doctors in China would be willing to perform surgeries such as those Jolie underwent without the presence of reliable symptoms or other evidence of disease: "A tense doctor-patient relationship undermines such preemptive, and therefore risky, medical procedures."

The well-defined genetic link to inherited disease demonstrated by Jolie is uncommon, but, in addition to breast and ovarian cancers, colorectal and medullary thyroid cancer can also be detected this way. "However, the risk for those two is not as high as for breast and ovarian cancers," he added.

He suggested that women who have been diagnosed with breast cancer should be screened for inherited BRCA genes because a positive result could warn other family members that they may also be at risk.

**Abnormal genes**

The majority of inherited breast cancers are associated with two abnormal genes, BRCA1 and BRCA2. Women who inherit a mutated version of either, irrespective of whether they came from their mother or father, have a much higher risk of developing breast and ovarian cancers.

Most people who develop breast cancer have no family history of the disease, but if there is a family history of breast or ovarian cancer, or both, genetics may have played a role in the development of the illness, experts said.

According to the United States National Cancer Institute, women with an abnormal BRCA1 or BRCA2 gene have an approximately 60 percent risk of being diagnosed with breast cancer, and the chances of developing ovarian cancer also rise. Generally for women, the risk is 12 to 13 percent. Abnormal BRCA1 or BRCA2 genes are found in 5 to 10 percent of breast cancer cases in the US, the institute said.

Ying said most public hospitals in China don't provide testing for BRCA genes because of a lack of effective and feasible interventions later on.

Zhao Ping, director-general of the Cancer Foundation of China, said genomic tests are useful because they can demonstrate a person's risk of developing certain types of cancer, but at present the knowledge is of little medical use.

"In the majority of cases, no further medical procedures can be undertaken, based merely on predictive genetic testing," he said. Zhao added that cancer is known to be caused by genetic mutation, but detection of "faulty" genes related to certain types of cancer doesn't necessarily mean that the patient will develop the disease.

He urged the health authorities to strengthen the regulations covering genomic testing, which is almost entirely unregulated by law or government guidelines.

Despite the doubts about the effectiveness of DNA testing, some researchers believe that it can still play a role in improving people's health.

Allied to other disease risk assessments, DNA tests may help physicians indentify the individuals at greatest risk, which allows targeted interventions, such as surgery, drug treatment and screening tests, said Wei Yingjie, a senior cardiologist in Heilongjiang province.

According to the World Health Organization, one-third of cancers are preventable, so changes to lifestyle and behavior are the keys to avoiding illness. Furthermore, raising a person's awareness of their genetic predisposition could prompt changes to their lifestyles, such as eating more healthily or stopping smoking.

Wei cautioned the public about using the genomic tests currently on the market for cardiovascular diseases. He said most heart conditions are caused by multi-gene-mutations and environmental factors, which can't be predicted. "Certain variant genes could be just a tiny part of all the risk factors," he said.

That means the vast majority of illnesses cannot be predicted with genomics, he said. There are only a few exceptions, including neural tube defects, which affect the brain, spine and spinal cord, and Marfan's syndrome, a condition that can affect cardiovascular and optical functions.

Wei said the results of genetic tests can be difficult to interpret, so specialists such as geneticists and genetics counselors must be brought in explain what the results could mean to an individual and their family members, but "China currently lacks genomics specialists of this type".

Rather than genomic tests, many doctors are urging the greater implementation of precision medicine - a new approach to treatment and prevention that takes individual variations of genes, environment and lifestyle into consideration - to improve the nation's health.

Yu Jun, a leading researcher in genomics and bioinformatics at the Beijing Genomics Institute at the Chinese Academy of Sciences, said a nationwide precision-medicine initiative is being planned to provide training in the relevant procedures.

Qin Huaijin, of the National Health and Family Planning Commission, said precision medicine is a huge and complex system that combines big data and personalized medicine: "It is definitely the future trend of medicine."

**Precision medicine initiative targets nation's health**

China has launched a strategic initiative to boost the use of precision medicine - treatments specifically designed for individual patients - that will receive government funding of 60 billion yuan ($9.2 billion) by 2030.

With a huge human gene bank as the foundation and gene-sequencing as the tool, the initiative aims to develop more-targeted diagnostics and treatments for specific diseases through advanced medical science and technology.

Major focuses will include cardiovascular disease, diabetes and selected cancers, which are currently the main killers in China, said Cao Xuetao, president of the Chinese Academy of Medical Sciences and Peking Union Medical College.

Cao said the essence of precision medicine centers on methods of prevention, diagnosis and treatment that take individual variability, particularly genomics (the study of the structure, function, evolution, and mapping of genomes), into consideration. Modern tools, such as genomics and bioinformatics - the collection and analysis of complex biological data, such as genetic codes - will help to achieve that.

"It will matter greatly to both the individual patient and the government because it can help provide the most effective treatments for individual patients and also reduce medical costs overall," he said.

To kick-start the initiative, the Chinese Academy of Sciences has solicited the first 4,000 volunteers for genetic studies, but that's just the beginning, according to Cao. "We are planning a gene data pool covering at least several million Chinese. The more data we have, the more precise the prevention and treatment will become," he said.

Francis S. Collins, director of the United States National Institute of Health, said collaboration will be the key to success.

"We'd like to cooperate with China in precision medicine. To bring these data sets together is the only way to make the collaboration work, and make the whole greater than the sum of its parts," he said.

"We are all one part of the family of human beings and we have to do it (develop the tests) together if we want to know important things about human health," he said.

In the long run, it will teach people more-effective ways to stay healthy and also save the government considerable expenditure on medical bills, he said.

"So there is also an economic driver here, to come up with ways of reducing healthcare costs," he added.

However, industry insiders said more preparation in relative research and rule setting concerning genetic data sharing will need to be undertaken before that can happen.

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