Migrant Studies Aid the Search for Factors Linked to Breast Cancer Risk

Breast cancer is by far the most common non-skin cancer in U.S. women. However, breast cancer rates vary widely around the world. Most cases occur in industrialized countries in Europe and North America, whereas the disease is less common among developing countries in Africa and Asia. Rates in the Netherlands, France, Denmark, and the United States, for example, cluster around 90–100 cases per 100,000 women, whereas those in China, India, Turkey, and Rwanda range from 10–20 cases per 100,000 women.

Over the past four decades, many studies have shown that breast cancer rates change when women move to a new country, providing evidence for the importance of lifestyle and environment in breast cancer risk. However, most of the studies have not been designed to answer questions about which factors are driving the increased risk.

Now, data from several recent studies of people who have migrated from their home countries are beginning to suggest some answers. “Migration provides a kind of natural experiment allowing the comparison of populations of similar genetic background living in different environments,” said Max Parkin, M.D., an epidemiologist at the University of Oxford in the United Kingdom.

Migrants typically move to countries with higher breast cancer rates than those of their country of origin. Two studies published in the 1990s showed that the Italian and Polish women had a higher risk of breast cancer after they migrated to Australia, where incidence rates are higher. Another study compared incidence rates of Japanese women who migrated to Los Angeles, San Francisco, and Hawaii to the rates of Japanese women still living in Japan. The incidence rates—63 per 100,000 in Los Angeles, 68 per 100,000 in San Francisco, and 73 per 100,000 in Hawaii—were more than twice as high as the rates for Japanese women living in Japan (24–31 per 100,000). A separate study showed that the third generation of Asian-American women living in the United States has rates similar to or greater than white women in the United States.

The factors frequently associated with these changes in breast cancer risk include “acculturation, Westernization of lifestyle, later marriage, fewer children later in life, changing infant feeding patterns, women getting taller, increasing rates of obesity, dietary changes, and exposures to carcinogenic agents,” according to a recent literature search of studies of breast cancer in migrant populations by Valentina Andreeva-Cook at the University of Southern California in Los Angeles.

Polish Women in the Midwest

To sort out which factors might affect breast cancer risk among such migrant
populations, Dorothy Rybaczyk Pathak, Ph.D., from Michigan State University in East Lansing, and the University of New Mexico in Albuquerque, and colleagues turned to the Polish migrant communities around Chicago and Detroit. Breast cancer incidence in these communities tripled within one generation, reaching the high rates of U.S.-born women. The rapid change in rates pointed to diet as a possible risk factor. Pathak presented the work at the American Association for Cancer Research’s prevention meeting in Baltimore in October.

In a case–control study among women within these communities, the researchers found that raw- or short-cooked cabbage and sauerkraut consumption (more than three servings per week) during adolescence and adulthood was associated with a 72% reduced risk of breast cancer compared with those who consumed 1.5 or fewer servings per week. Consumption of long-cooked traditional Polish dishes, such as hunter’s stew, cabbage rolls, and pierogies, had no effect on risk.

The inverse association was strongest when consumption occurred in adolescence, even if the women did not continue to consume large amounts during adulthood. High consumption during adulthood was also associated with reduced breast cancer risk, even for women who ate intermediate or small amounts during adolescence.

“This is a unique population,” said Pathak, herself a Polish-born American. “Poles consume cabbage in many forms, and a lot of it—three times more than Americans. Working with the migrant population allowed us to study the effect of a wide range of exposures to cabbage that can’t be found in the U.S. population.”

Cabbage is a cruciferous vegetable, which includes broccoli, Brussels sprouts, kale, collard greens, and cauliflower. These plants contain glucosinolates that break down in the body into products with anticarcinogenic properties. Cooking decreases the bioavailability of these agents, which have been shown to reduce the risk of various cancers in both animal and human studies.

“Observing the effect for only the raw or lightly cooked [vegetables] fits well with the bioavailability of these compounds in our diet,” Pathak said.

**Chinese, Japanese, and Filipinos in Los Angeles**

Anna H. Wu, Ph.D., at the Department of Preventive Medicine, University of Southern California in Los Angeles, has also studied diet in migrant populations. In a case–control study among Chinese, Japanese, and Filipina women in Los Angeles County, Wu reported in 2003 that those who drank the most green tea daily had about a 50% reduced risk compared with women who drank green tea less than once a month. The level of green tea consumed in this migrant population, however, was four to five times lower than in Japan where several cups, or about 400–500 mL, are consumed daily. (An average cup of tea is 120 mL.)

Previous studies in Western populations of people who drink primarily black tea have found no association between tea consumption and risk of breast cancer. Wu said she believes a better understanding is needed to determine how the amount of green tea consumed affects cancer risk. Also, it is not well understood how different types of tea and methods of preparation affect the concentration of tea polyphenols, the presumed anticancer agents in green tea.

Another component of the traditional Asian diet, soy, may also play a protective role in breast cancer risk, according to Wu. In the same population of Asian-American women, she reported in 2002 that women with the highest soy intake during adolescent and adult life had about a 50% reduced risk of cancer compared with those who were low consumers in both periods. Some studies have shown that soy isoflavones have anticancer properties. The average intake of isoflavones in this population of Asian Americans was 12 mg per day. In comparison, the Chinese in Shanghai, whose breast cancer rate is about one-third less than the rate among Chinese women in Los Angeles, consume about 33 mg per day.

In this issue of the Journal (see article, p. 459), Bruce J. Trock, Ph.D., of the Johns Hopkins School of Medicine in Baltimore, and colleagues, attempt to further quantify the association between soy intake and breast cancer risk. Their meta-analysis highlights both the great deal of attention the potential relationship has received and the complexity of studying any dietary risk factor in various populations. “Considered as a body of evidence, these studies support a small reduction in breast cancer risk associated with intake of soy foods, although interpretation of these results is tempered by lack of a dose response and inconsistencies in the data,” they write.

**Chinese in Philadelphia**

Marilyn Tseng, Ph.D., and her colleagues from the Fox Chase Cancer Center in Philadelphia, looked at many breast cancer risk factors for Chinese-born women living in Philadelphia. Her work, also presented at the fall AACR prevention meeting, found an association between breast density and degree of acculturation among 250 recent immigrants. Acculturation refers to English proficiency and degree of social and professional interactions with Americans.

“We used breast density as an intermediate marker for breast cancer risk
because there is a strong association between breast density and breast cancer risk,” said Tseng.

When she found that the women in the highest category of acculturation were more likely to have denser breasts, she looked for factors responsible for the association. But none of the factors associated with a high degree of acculturation—better education, fewer live births, higher age at first live birth, short duration of breastfeeding, higher intake of dairy foods and chicken, lower intake of folic acid, more likely to have a first degree relative with breast cancer, more likely to have used oral contraceptives and hormone therapy—could account for the relationship between acculturation and breast density.

“It may be that we are measuring exposures at the wrong period of time,” she said. “Perhaps there are exposures that happen during peri-menopause [the time between pre- and postmenopause], or that occur immediately after migrations that we need to look at.”

Tseng has already started recruiting for another study that will include 420 recent immigrants between ages 39 and 50.

“This time we’ll be collecting the same data three times over a 3-year period,” she said. “Hopefully, this will allow us to probe more sensitively into which changes in lifestyle are linked to changes in breast density. It’s a time when changes are happening so quickly in the migrant population.”

**Risk Factors for Breast Cancer**

Many of the known risk factors for breast cancer may explain some rate differences across ethnic groups, such as those between Latina women from Mexico and South and Central America compared to U.S. whites. According to Malcolm Pike, Ph.D., and his colleagues at USC, the 40% lower rates amongLatinas are due in part to later age at menarche, younger age at first birth, greater number of children, and low postmenopausal hormone replacement therapy and alcohol use.

However, since the known risk factors for breast cancer account for only about 60% of the risk, there is still much work to be done and good reason to believe that migrant studies will continue to shed light on which factors are important.

“The contribution of migrant populations is unique,” said Wu. “Whether you’re talking about Asians or Latinos to the U.S., or European migrants to Australia, migrant populations take their lifestyle, diet, and many other factors with them to their adopted countries. As they acculturate and begin to acquire the habits of the host country, over time, they experience a very wide range of exposures to environmental factors and are therefore particularly informative.”

——Nancy J. Nelson

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