Advanced Breast Cancer in Young Women

By Judy Peres

A recent study in the *Journal of the American Medical Association* disturbed young women. The study, which all the major media picked up, found that the incidence of advanced breast cancer in women younger than 40 years had nearly doubled over three decades.

But the importance of the finding, which the authors admit needs confirmation, remains a mystery, and some experts question whether it’s real.

“It could be explained simply by multiple looks at the data,” said Peter Ravdin, M.D., Ph.D., director of the Breast Health Clinic at the University of Texas Health Science Center at San Antonio. “The researchers were doing an exploratory analysis [as opposed to testing a hypothesis], so the p values [of statistical significance] appear stronger than they really are.”

“Observational studies can be misleading,” agreed Donald Berry, Ph.D., professor of biostatistics at the University of Texas M. D. Anderson Cancer Center in Houston. “If you look hard enough through a large amount of data, you’ll find things that seem unusual.”

The analysis of data from the National Cancer Institute’s Surveillance, Epidemiology, and End Results (SEER) database found that the incidence of advanced breast cancer—tumors that have already metastasized to distant sites at time of diagnosis—has statistically significantly increased in women younger than 40 years, especially hormone-sensitive cancer. The researchers found no increase in older age groups or in less-advanced disease in the under-40 group.

Specifically, the incidence rate for 25- to 39-year-old women climbed from 1.53 per 100,000 in 1976 to 2.90 per 100,000 in 2009—and the increase appeared to be accelerating: “The trajectory of the incidence trends predicts that an increasing number of young women in the United States will present with metastatic breast cancer in an age group that already has the worst prognosis, no recommended routine screening practice, the least health insurance, and the most potential years of life,” the authors concluded.

The *JAMA* article (Feb. 27) carried more poignancy: Its first author, Rebecca Johnson, M.D., director of the adolescent and young-adult oncology program at Seattle Children’s Hospital, was diagnosed with breast cancer 17 years ago, at age 27.


Experts quickly admonished that routine mammography screening is not appropriate for women younger than 40 years, which is one of the conundrums of the paper.

“The principal observation of this article is a curiosity,” said Berry, “but it has no policy or clinical implications. It doesn’t begin to imply that women in this age group should be screened, for example, and not even the authors suggest that.”

Johnson and coauthor Archie Bleyer, M.D., do suggest that women of all ages report any change in their breasts to a physician. “I hope our publication increases that awareness that you can’t ignore a lump, discharge, or pain,” said Bleyer, clinical research professor at Oregon Health and Science University in Portland.

Berry agreed with that message, but with an important caveat: “It’s far from clear that treating it [at the point where symptoms are apparent] would change the outcome. It’s quite conceivable that the cat is already out of the bag,” that is, the tumor has already spread to distant organs.

Johnson stressed that her research was “very preliminary. The trend we identified needs to be validated in other large databases—colleagues in Canada are already looking—and then we’ll look at what might be underlying the trend. Are there environmental factors? Modifiable lifestyle factors? That will require a series of hypothesis-based research projects.”

Bleyer said that no one knows what might be causing the increase. “It’s probably a combination of factors: increased obesity, later childbirth, decreased or later breast-feeding, earlier menarche, and other aspects yet to be identified,” he said.

Even if the effect is real, the numbers are small. In absolute terms, about 250 cases of metastatic breast cancer were diagnosed in U.S. women aged 25–39 years in 1976, compared with about 850 today. (The overall number of women in that age group went from about 22 million to about 30 million over the same period.) The increase in the incidence rate, from 1.53 to 2.90 cases per 100,000, or 1.37 case patients, could be caused by such factors as improved staging due to positron emission tomography scans and other sophisticated diagnostic imaging. “Better staging would easily explain all 1.37 [case patients] per 100,000,” said Berry.

Screening might also contribute. “Not many women aged 25–39 get screened,” said Berry, “but some do. It takes only a few to account for a statistically significant increase from 1 in 100,000.”

One expert who is less inclined to explain away the *JAMA* findings is the National Cancer Institute’s William F. Anderson, M.D., M.P.H. Anderson, a senior scientist in the biostatistics branch of the Division of Cancer Control and Population Sciences at the National Cancer Institute’s William F. Anderson, M.D., M.P.H. Anderson, a senior scientist in the biostatistics branch of the Division of Cancer Control and Population Sciences.
Researchers Link Early Hair Loss and Prostate Cancer

By Mike Fillon

Accoding to a few new studies, men who lose their hair early in life have a greater risk of developing prostate cancer—especially African American men.

Although researchers have long suspected a link between baldness and prostate cancer, earlier studies have been inconclusive—and sometimes conflicting. (JNCI reported on the potential link in the early 1970s.)

In October 2008, researchers from the Division of Cancer Epidemiology and Genetics at the National Cancer Institute published “Androgen and Prostate Cancer: Is the Hypothesis Dead?” in Cancer Epidemiology, Biomarkers, and Prevention. They said that although data from animal, clinical, and prevention studies support the role of androgen in prostate cancer growth, proliferation, and progression, “results from serum-based epidemiologic studies in humans have been inconclusive, and... showed no association between serum androgen and prostate cancer risk.”

That same year, a study from Istanbul, Turkey, amplified this conclusion. Published in volume 11 of Informa Healthcare, their study of 152 patients found no correlation between pattern of baldness and androgen levels in the blood.

However, researchers from the European Georges Pompidou Hospital in Paris, France, reached a different conclusion. Reporting on a study of 669 subjects in the Aug. 22, 2011, issue of Annals of Oncology, they found that patients with prostate cancer were twice as likely to have male pattern baldness, or androgenic alopecia (AA), at age 20 years.

ER-positive cancers might contribute to the reduction in ER-negative disease. At the same time, he said, “statistically significantly different birth cohort deviations for ER-positive and ER-negative cancers are consistent with different trends in etiologically distinct entities.” Anderson said that these patterns need to be confirmed but added, “If it is truly a cohort effect, certain reproductive, dietary, and hormonal risk factors must do different things to ER-positive and ER-negative breast cancers.” For an example, he pointed to childbearing: “As parity goes down, ER-positive disease goes up while ER-negative disease goes down.”

Ravdin said that obesity, too, could have a dual effect. He noted that results from the P-1 Breast Cancer Prevention Trial showed that obesity selectively increases the proportion of ER-positive breast cancer in premenopausal but not postmenopausal women. Then he added, “Perhaps speculating about the mechanisms of an effect that arguably may or may not be real is getting ahead of the game.”

© Oxford University Press 2013. DOI:10.1093/jnci/djt245