

Dense breasts, hormone levels are 2 separate, independent risk factors for breast cancer

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The density of a woman's breast tissue and her level of sex hormones are two strong and independent risk factors for breast cancer, according to a team of researchers from Harvard and Georgetown universities. The finding dispels the common belief that the risk associated with dense breasts merely reflects the same risk associated with high levels of circulating sex hormones, they say.

Their study, published in the August 1 issue of the *Journal of the National Cancer Institute*, found that the relative risk of developing breast cancer in post-menopausal woman with dense breasts was 400 percent higher than in women with fatty, non-dense breast tissue, and that high versus low levels of hormones (estrogen and testosterone) increased the relative risk by 200 percent. Adjusting for a woman's circulating hormone levels did not reduce the risk associated with the level of breast density. Furthermore, these independent risk factors seemed to have additive effects so if a woman had both dense breasts and excess hormones, her risk was increased by 600 percent, the researchers found.

“We have found that dense breasts are not a marker for higher hormone levels, or vice versa, and this tells us each increases breast cancer risk via a different biochemical pathway,” said co-author Celia Byrne, Ph.D., an assistant professor in the Lombardi Comprehensive Cancer Center at Georgetown University Medical Center. Byrne designed and conducted the study while she was an instructor of medicine at Harvard Medical School. The study's three other authors, including the corresponding author, Rulla Tamini, Sc.D., were from Harvard.

Women at risk should pay attention to these early findings, even though they need to be confirmed and studied further, Byrne added. “Women who know they have dense breasts should make sure they have regular mammograms,” she said. Women usually don’t know if they have dense breast tissue and the best way to find out is through a digital mammogram, she explained. Additionally, post-menopausal women who are overweight can reduce their blood hormone levels by decreasing body fat, Byrne added, since fat itself is converted by the body to estrogen.

The findings represent an opportunity to both fine-tune existing breast cancer risk models, which, thanks to research by Byrne and her colleagues, now include breast density to help estimate a woman’s risk. But the model does not take into account hormone level, Byrne said. “If we could find out what causes breast tissue to be dense, and how that increases breast cancer risk, then we might have a new opportunity to help women lower their risk,” she said.

Byrne said she was surprised at the findings. “Our assumption was that this study would confirm what everyone had believed – that hormone levels explain breast density.” This presumption of an association between hormone levels and breast density was based on “the circumstantial evidence, such as the fact that during pregnancy, when hormones increase, breasts also grow in size,” she said. “But that is not what our study showed.”

In a 1995 study, Byrne and her colleagues discovered that women whose breasts contain at least 75 percent dense tissue are at a four- to six-fold greater risk of breast cancer than women with entirely fatty breasts (no measurable dense tissue). Recent research has suggested that having dense breast tissue may be partially an inherited genetic trait. Other recent studies have indicated that for women with dense breast digital mammography may be more effective for screening.

In this study of 773 postmenopausal women who participated in Harvard's Nurses Health Study –253 who had breast cancer and 520 who didn't – the researchers evaluated hormones in their blood and measured breast density using a computer-assisted analysis of mammograms. None of the women were using hormone replacement therapy (HRT) at the time they were evaluated.

There are several theories as to why dense breasts might increase a woman's risk of developing breast cancer, Byrne said. One is that dense tissue has more epithelial cells than breasts that are not dense, and thus more possibilities exist that one or more of these cells will become cancerous. Another is that there is more "cross-talk" between the stromal cells in the breast, which produce a variety of hormones and growth factors, and epithelial cells in the tissue, which is where most breast cancer develops. The third is a combination of the first two theories, she said.

Much more work needs to be done to understand why breast density would increase breast cancer risk, the researchers wrote, and they noted that further studies should measure hormone levels directly within breast tissue, not indirectly through blood, as they chose to do in this first investigation.

Source: Georgetown University Medical Center

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