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8 insights on lobular breast cancer

Historically, two [breast cancer](#) subtypes known as invasive lobular carcinoma and ductal carcinoma have been grouped together. They've been thought of as having the same screening needs, symptoms, genetic drivers and treatment. But that's a mistake.

A [recently published comprehensive review](#) and new research being presented at the [2022 American Society of Clinical Oncology Annual Meeting \(ASCO\)](#) by breast medical oncologist [Jason Mouabbi, M.D.](#), is helping to distinguish invasive lobular carcinoma as its own subtype and define more tailored treatment approaches.

Invasive lobular carcinoma is different from ductal carcinoma

Invasive lobular carcinoma, also called lobular breast cancer, forms in the cells of the breast that produce milk. These cells are called lobules. When breast cancer occurs in the cells of the milk ducts and/or the nipple, the diagnosis is classified as ductal carcinoma.

"These cells have such different functions. How could we study them as one?" Mouabbi says. Though both occur in the breast, the diagnoses are very different.

Invasive lobular carcinoma isn't rare

Lobular breast cancer accounts for only 10% of breast cancer cases in the United States. It's been seen as impractical to study the subtype separately, Mouabbi says.

However, 40,000 women will face a lobular breast cancer diagnosis this year. That's more cases than [ovarian](#) and [cervical cancer](#), which are estimated to have 29,000 and 19,000 cases this year, respectively.

"It's wrong to say it's a small proportion of cancers," Mouabbi argues. "It's a small portion of breast cancers, but it's a sizable population facing this diagnosis each year." Because of the number of diagnoses each year, Mouabbi says it's important to conduct studies devoted to the subtype to improve care. "It needs to have more attention so we can find better screening, better detection and better therapies," Mouabbi says.



We've identified targets that may lead to more effective treatment.

Jason Mouabbi, M.D.
 Physician & Researcher

Lobular breast cancer doesn't always present as a mass

"It's a myth that breast cancer always shows up as a mass," Mouabbi says. While ductal breast cancer grows like an onion, lobular breast cancer doesn't.

"One of the hallmarks of lobular breast cancer is that it loses its anchoring protein," Mouabbi says. The cancer cells don't link with surrounding cells so they grow in lines. Eventually, the lines of cancer cells cross and interconnect to form a mass, but at that point, the cancer is advanced.

Because the cancer doesn't grow as a mass, patients often can't feel it. Those who do report their breast feel denser or they see their nipple retract.

[Mammograms and ultrasounds](#) also aren't effective in detecting the cancer because of its cell growth pattern. The best screening approach is a breast MRI, which isn't standard of care.

“Until MRI becomes more widely used, I’m afraid that lobular cancer is going to be underdetected,” Mouabbi says. Because detection is challenging and patients don’t see changes in their breast, 60% to 70% of patients’ diagnoses are changed to a higher stage after surgery.

Mouabbi says it’s common for patients to be initially diagnosed with a mass that’s less than 1 centimeter but is found to be much larger at surgery.

Lobular breast cancer spreads to the gastrointestinal and urinary tracts

Lobular breast cancer tends to spread to unusual sites, such as the lining of the gastrointestinal and urinary tracts. Patients often notice they feel constipated or have changes with urination.

Like in the breast, the cancer cells grow linearly and cause these tracts to narrow. “It’s like a lasso that tightens over time,” Mouabbi says.

Because the cells grow in sheets and not a mass, metastasis is also difficult to detect.

Family history can help determine risk of lobular breast cancer

There are trends that can help identify people are at higher risk for invasive lobular carcinoma.

Individuals with a family member who has also been diagnosed with the disease are at a higher risk of the same diagnosis, Mouabbi says.

In addition, people with a family history of [stomach cancer](#) face a greater risk of lobular breast cancer. “It’s the same mutation fueling the cancers,” Mouabbi says.

Lastly, the precancerous lesion known as lobular carcinoma *in situ* (LCIS) can increase a person’s chances of a lobular breast cancer diagnosis. With LCIS, the abnormal cells grow inside the lobule, but because they’re contained, it’s considered premalignant. They can also become [calcified](#), which allows detection with a mammogram and surgical removal. “But patients often aren’t aware that LCIS spots increase their risk of lobular breast cancer in both breasts,” Mouabbi says.

Standard of care treatment not tailored to invasive lobular carcinoma

To help identify lobular breast cancer early, Mouabbi urges patients who fall into these categories be monitored with an MRI rather than an ultrasound.

Many patients with invasive lobular carcinoma receive the standard-of-care [chemotherapy](#), but the comprehensive review showed there isn’t much clinical benefit. That’s because it has been based on clinical trials combining lobular and ductal breast cancer. “All the conclusions from these studies are driven by ductal carcinoma,” Mouabbi says. “We need something different for these patients.”

He adds that prognostic tools such as Oncotype DX and MammaPrint are not very useful in invasive lobular carcinoma for the same reasons. “While it’s been thought that invasive lobular has a favorable prognosis when compared to ductal carcinoma, our review showed that’s not true in the long-term,” Mouabbi says.

Endocrine therapy is effective in treating invasive lobular carcinoma

There are other therapies for invasive lobular carcinoma, but they’re not widely used yet. For example, the review led by Mouabbi found that 95% of lobular breast cancers are hormone-driven, while only about 50% of ductal breast cancer are. Because of this, lobular breast cancer can be treated with endocrine therapy.

Also, lobular breast cancer appears to be immunologically hot. That means the immune system recognizes the tumor. Mouabbi hopes to open [clinical trials](#) at MD Anderson soon to investigate treating these cancers with [immunotherapy](#).

Other opportunities lie in the genomic makeup of the cancer. “We found that lobular breast cancers are universally driven by the *CDH1* mutation,” Mouabbi says. They also found almost 15% of patients carry the HER2 gene mutation, and 60% carry the PIK3CA gene mutation.

“It’s exciting because we’ve identified targets that may lead to more effective treatment,” Mouabbi says. And the mutations are present at conception. This means targeted therapies could be an option for initial treatment. The retrospective analysis being presented by Mouabbi at the 2022 ASCO Annual Meeting reveals targeted therapy outcomes in patients with lobular breast cancer. “We found that patients benefit from a combination of targeted therapy and endocrine therapy,” Mouabbi says.

Invasive lobular carcinoma clinical trials are critical for progress

To define more personalized approaches, Mouabbi says it’s critical to conduct clinical trials specific to lobular breast cancer. Or, if clinical trials are combined, the patients must be protected with a cohort specific to the subtype.

“If there’s a clinical trial specific to lobular breast cancer, I urge patients to consider enrolling,” Mouabbi says. “It all starts by building more awareness about this disease.”