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# Young Women Face Difficult Breast Cancer Care Choices—But Extensive Surgery May Not Save Lives

## New Data Challenges Assumptions About Mastectomy for Young Breast Cancer Patients with High-Risk Disease

***Abstract: Surgical Management of Young Women with High-Risk Breast Cancer Receiving Neoadjuvant Systemic Therapy***

**Seattle, WA, May 1, 2026—**Whether treated with mastectomy or lumpectomy, young women with locally advanced breast cancer treated with neoadjuvant systemic therapy experienced similar outcomes but underwent more extensive surgical treatments than older patients with similar disease in a new study presented this week at The American Society of Breast Surgeons (ASBrS) Annual Meeting in Seattle.

After adjusting for tumor clinical characteristics and systemic therapy response, researchers examined trends in surgical breast cancer management in I-SPY2 clinical trial data grouped by patients age 45 and younger, and over age 45.

This study is significant because it is one of the few that specifically focuses on high-risk breast cancers in a young population and the impact of the growing number of effective neoadjuvant breast cancer therapies available today. It also elucidates new trends in breast cancer treatment and outcomes in younger populations during the past decade, as disease rates climb and studies are lacking. Significantly, it leverages data from a large, multi-center, randomized trial with high reliability.

Noting that for young women, in particular, breast cancer treatment is a life-altering decision and should be informed by the latest knowledge and research, lead researcher Jennifer Tseng, M.D., Associate Clinical Professor and the Medical Director of Breast Surgery at City of Hope Orange County, CA, says, “Unfortunately, despite similar recurrence and survival rates for comparable disease, younger patients more often undergo mastectomy, which excises all breast tissue, rather than breast conserving surgery,

which removes only the tumor along with a surrounding margin of healthy tissue and has lower rates of complications and morbidity along with higher patient satisfaction."

"Younger women and some of their physicians may equate more extensive treatment with long-term survival when this may not be the case," she says.

In this study, even for high-risk patients, mastectomy provided no benefits in recurrence prevention or overall survival. The research also suggests that neoadjuvant therapies in this population may be an important and possibly overlooked strategy to alter a tumor profile, making patients who would otherwise be treated with mastectomy appropriate for lumpectomy.

Studies such as this, Dr. Tseng believes, are important to alter assumptions about cancer therapy in young women and drive a reexamination of the benefits of surgical de-escalation.

The study examined 1,737 patients participating in the I-SPY2 trial from April 2010 to June 2022 with a follow-up of approximately five years. Of these, 698 (40.2%) were age 45 or younger and 1,039 (59.8%) were older than age 45. All patients had clinical stage II-III breast cancer with high-risk MammaPrint scores. MRI functional tumor volumes (FTV) before and after neoadjuvant systemic therapy were calculated to assess therapy impact.

Statistical associations used included Wilcoxon rank-sum, Pearson's Chi-squared, Fisher's exact and Kruskal-Wallis tests. Overall survival and locoregional free interval (local recurrence and in lymph) were assessed with Kaplan-Meier method, log-rank test and multivariate Cox proportional hazard regression models, adjusting for patient and clinical factors of tumor subtype, clinical T category, clinical nodal status, histologic grade, breast/axillary surgeries and Residual Cancer Burden (RCB) Class.

Researchers found that tumor features, nodal status and histologic grade were similar across age groups. Patients age 45 or less had greater MRI FTV before (32.88 cm3 vs 23.02 cm3, $p<0.001$) and after (4.60 cm3 vs 3.22 cm3, $p<0.001$) neoadjuvant systemic therapy.

Notably, rates of breast conserving surgery were lower in those age 45 and younger compared to patients older than 45 years (36.8% vs 48.5%, $p<0.001$). On multivariate analysis, no significant differences were found in survival or local recurrence for patients in the younger age group undergoing breast-conserving surgery compared to mastectomy.

"More research is needed to identify the appropriate treatment protocols for younger patients," says Dr. Tseng. "Additionally, existing information may not be readily accessible to patients and the complete medical community involved in their care. For this population, in particular, communications and information sharing are powerful cancer care tools."

**Surgical Management of Young Women with High-Risk Breast Cancer Receiving Neoadjuvant Systemic Therapy**

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**Background/Objective:** Despite breast-conserving therapy having been found to be equivalent to mastectomy for many patients with early-stage breast cancer, mastectomy rates continue to be higher in younger women compared to older women. The impact of this more extensive breast surgery on overall survival and local recurrence in younger women is unknown, especially after neoadjuvant systemic therapy. The goal of this study was to evaluate the trends and outcomes in the surgical management of patients age ≤45 years vs >45 years enrolled in the I-SPY2 clinical trial, a multicenter neoadjuvant systemic therapy platform trial.

**Methods:** Clinical and pathological factors were reviewed comparing patients age ≤45 years vs >45 years with clinical stage II-III breast cancer enrolled in the I-SPY2 clinical trial from April 2010 through June 2022. All patients enrolled had tumors with high-risk MammaPrint scores. MRI functional tumor volumes (FTV) before and after neoadjuvant systemic therapy were calculated. FTV is a quantitative imaging biomarker measured on contrast-enhanced breast MRI based on the quantity of tissue within the tumor meeting enhancement thresholds. Surgical therapy was categorized as 1) breast-conserving surgery (BCS) vs mastectomy, and 2) sentinel node surgery (SN) vs axillary lymph node dissection (ALND). For associations between continuous baseline characteristics and age groups, the Wilcoxon rank-sum test was used. For associations between categorical baseline characteristics and age groups, Pearson's Chi-squared test and Fisher's exact test were used. Associations of age groups with overall survival (OS) and local recurrence-free interval (LRFI) were examined with the Kaplan-Meier method, log-rank test, and multivariate Cox proportional hazard regression models, adjusting for patient and clinical factors of tumor subtype, clinical T category, clinical nodal status, histologic grade, breast/axillary surgeries, and Residual Cancer Burden (RCB) Class.

**Results:** There were 1737 patients included in this study, with 698 (40.2%) age ≤45 years and 1,039 (59.8%) age >45 years. There were no significant differences in patient characteristics of self-reported race/ethnicity or tumor features such as receptor subtype (HR+HER2 negative, HER2 positive, or triple-negative), clinical tumor/nodal categories, or histologic grade by age groups. RCB class distribution after NAC was also similar between age groups. Patients age ≤45 years had greater MRI FTV before (32.88 cm3 vs 23.02 cm3, p<0.001) and after (4.60 cm3 vs 3.22 cm3, p<0.001) neoadjuvant systemic therapy. Rates of BCS were lower in those age ≤45 years than patients older than 45 years (36.8% vs 48.5%, p<0.001). There were no significant differences in extent of axillary surgery between age groups (SN: 65.0% vs 65.4%; ALND: 35.0% vs 34.6%, p=0.9). Median time to last follow-up or death was 5.24 years,

with 200 OS events (≤45: 80; >45: 120) and 133 LRFI events (≤45: 58; >45: 75). On multivariate analysis, there were no significant differences in OS or LRFI for patients aged ≤45 years undergoing breast-conserving surgery vs mastectomy for surgical management. For patients age ≤45 years, there was no significant difference in OS by breast surgery across tumor subtypes, although BCS was associated with better LRFI within the HR+HER2 negative subtype (p=0.047).

**Conclusion:** Young women with locoregionally advanced, high-risk breast cancer in the I-SPY2 clinical trial had higher FTV on breast MRI and lower rates of breast-conserving surgery than older women. Importantly, the extent of breast surgery did not impact overall survival or locoregional recurrence in women age ≤45 after adjusting for other clinical characteristics and response. The choice of surgical procedure in the management of breast cancer is multifactorial, but young age does not necessarily warrant mastectomy following neoadjuvant systemic therapy.