SOUTHERN SURGICAL ASSOCIATION ARTICLE

Multigene Signature Panels and Breast Cancer Therapy: Patterns of Use and Impact on Clinical Decision Making

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BACKGROUND: A growing body of evidence supports the use of multigene signature panels (MSPs) in predicting recurrence risk in patients with invasive breast cancer. This study aimed to evaluate trends in MSP use over time and the effect of MSPs on administration of postoperative chemotherapy.

STUDY DESIGN: The National Cancer Database was queried for all women with invasive breast cancer who underwent resection between 2011 and 2014 and had information about performance of an MSP, hormone receptor status, and receipt of chemotherapy. Multigene signature panel use over time was evaluated, and patterns of use of Oncotype DX (ODX) and MammaPrint (MP) were compared.

RESULTS: In a total of 476,128 patients, an MSP was obtained in 153,782 (30.2%). Multigene signature panel use increased over time and was associated with a decreased rate of chemotherapy administration (24.6% MSP vs 37.2% no MSP; $p < 0.001$). Oncotype DX remained the most common MSP used throughout the study period. Oncotype DX was used more commonly in stage I disease than MP, and MP was used more commonly in stage II and III disease. MammaPrint was more commonly used in hormone receptor-negative patients, human epidermal growth factor receptor 2-positive patients, and patients with positive lymph nodes. Postoperative chemotherapy was administered to a higher proportion of patients assessed with MP than with ODX (41.3% vs 23.4%, respectively; $p < 0.001$).

CONCLUSIONS: Use of MSPs among patients with breast cancer has increased over time and is associated with a decreased use of adjuvant chemotherapy. Oncotype DX continues to be the most widely used MSP, although MP use has increased over time. Future studies are warranted to determine the optimal use of these MSPs in risk assessment and postoperative decision making. (J Am Coll Surg 2018;■:1−7. © 2018 by the American College of Surgeons. Published by Elsevier Inc. All rights reserved.)

Multigene signature panels have become widely used in evaluating patients with early stage (I or II) breast cancer, with the hope of better assessing prognosis and guiding therapy.[1-4] The 2 most prominent multigene signature panels (MSPs), Oncotype DX (ODX, a 21 gene panel comprising genes involved in estrogen signaling)[5] and MammaPrint (MP, a panel based on the Amsterdam 70-gene breast cancer gene signature)[6] both have demonstrated efficacy for evaluation of recurrence risk in women with stage I, II, or IIIa breast cancer with or without positive lymph nodes.

In the US, ODX represents the only such tool supported by the National Comprehensive Network for women with early stage, estrogen receptor (ER)-positive tumors.[7] By stratifying patients into groups of low, intermediate, or high risk of recurrence, it aims to guide clinicians in identifying those patients in whom postoperative chemotherapy in addition to hormone therapy would be

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Abbreviations and Acronyms

ER = estrogen receptor
HER2 = human epidermal growth factor receptor 2
MP = MammaPrint
MSP = multigene signature panel
ODX = Oncotype DX

beneficial and outweigh the side effects. Evidence also suggests that ODX score also correlates with breast cancer-specific mortality.[8] Although MP has not yet been endorsed by the National Comprehensive Network, it applies to a wider variety of early-stage breast cancer patients—namely those with early stage (I or II) breast cancer regardless of ER status.

Studies comparing the 2 platforms, ODX and MP, have largely focused on comparative accuracy in predicting recurrence.[9,10] To date, no large-scale study has assessed trends in MSP use over time, the impact of MSP use on the proportion of patients receiving adjuvant chemotherapy, or differences in usage and impact on clinical decision making between ODX and MP. This study aims to answer those questions and understand how these powerful tools are being used in the treatment of patients with early-stage breast cancer in the US.

METHODS

Patient selection

The National Cancer Database, a comprehensive clinical oncology database compiled from de-identified patient data from more than 1,500 Commission on Cancer-accredited hospitals, was queried for all women diagnosed with invasive breast cancer between 2011 and 2014. Patients were included if they underwent surgical resection for invasive breast cancer and had information about performance of an MSP, ER status, and information about receipt of chemotherapy. A schematic detailing patient selection from the National Cancer Database is shown in eFigure 1.

Multigene signature panel use and outcomes

Use of MSPs over time was evaluated along with the relationship between demographic and tumor characteristics and the use of MSPs. Receipt of adjuvant chemotherapy was assessed among patients in whom an MSP was and was not performed after excluding patients who received neoadjuvant chemotherapy or those in whom chemotherapy sequence was not known. The 2 groups were compared to assess the impact of MSP use on the decision to administer postoperative chemotherapy. Type of MSP was then evaluated among patients in whom an MSP was performed. Frequency of ODX and MP was assessed in the whole MSP cohort. Use of ODX and MP was then compared with respect to TNM stage at diagnosis, hormone receptor status, human epidermal growth factor receptor 2 (HER2) status, lymph node status, and the proportion of patients undergoing each test who received postoperative systemic chemotherapy. Finally, administration of adjuvant chemotherapy was compared based on ODX and MP test results, with cutoffs for recurrence risk based on manufacturer recommendations and prospective randomized trials.

Statistical analyses

Univariate analysis was performed using chi-square tests for contingency tables, Pearson correlation for evaluation of trends in MSP use over time, and logistic regression for assessment of the relationship between continuous variables and the use of MSP. For all analyses, $p < 0.05$ was considered significant. All analyses were performed with SAS software, version 9.4 (SAS Institute).

RESULTS

Among 476,128 women included in the study dataset, an MSP was obtained in 153,782 (30.2%). Demographic and clinicopathologic details for the entire cohort are listed in Table 1. Briefly, median age was 61 years, and most patients were white, had stage I to II disease, and were ER-positive. Multigene signature panels use increased over time from 2011 (29.7%) to 2014 (34.4%) ($p = 0.005$) (Figure 1). Overall, patients in whom an MSP was obtained were younger, more likely to be white, and more likely to have private insurance (Table 2). Additionally, they most often had stage I or II disease and had hormone receptor-positive and HER2-negative tumors.

During the study period, MSP use was associated with a decreased rate of chemotherapy administration (24.6% MSP vs 37.2% no MSP; $p < 0.001$). The greatest rates of decrease in chemotherapy administration among patients undergoing genetic assessment with an MSP occurred among patients with stage II disease (33.9% among MSP patients vs 60.7% among non-MSP patients; $p < 0.001$) and stage III disease (62.1% among MSP patients vs 77.6% among non-MSP patients; $p < 0.001$) (Table 3).

Among MSPs, ODX remained the most common test used throughout the study period (94.9% to 92.7% of all MSPs used from 2011 to 2014), although the use of MP increased over time (2.3% to 4.7% of all MSPs used from 2011 to 2014; $p = 0.03$) (Figure 2). Although ODX use was more common in patients with stage I disease than