Original Article

Chemotherapy Decisions and Patient Experience With the Recurrence Score Assay for Early-Stage Breast Cancer

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BACKGROUND: The 21-gene recurrence score (RS) assay stratifies early-stage, estrogen receptor–positive breast cancer by recurrence risk. Few studies have examined the ways in which physicians use the RS to recommend adjuvant systemic chemotherapy or patients' experiences with testing and decision making. **METHODS:** This study surveyed 3880 women treated for breast cancer in 2013-2014; they were identified from the Los Angeles County and Georgia Surveillance, Epidemiology, and End Results registries (response rate, 71%). Women reported chemotherapy recommendations, the receipt of chemotherapy, testing experiences, and decision satisfaction. Registries linked the tumor data, RS, and surveys. Regression models examined factors associated with chemotherapy recommendations and receipt by the RS and subgroups. **RESULTS:** There were 1527 patients with stage I/II, estrogen receptor/progesterone receptor–positive, human epidermal growth factor 2–negative disease: 778 received an RS (62.6% of patients with node-negative, favorable disease, 24.3% of patients with node-negative, unfavorable disease, and 13.0% of patients with node-positive disease; $P<.001$). Overall, 47.2% of the patients received a recommendation against chemotherapy, and 40.5% received a recommendation for it. RS results correlated with recommendations: nearly all patients with high scores (31-100) received a chemotherapy recommendation (86.9%-96.5% across clinical subgroups), whereas the majority of the patients with low-risk results (0-18) received a recommendation against it (65.9%-78.2% across subgroups). Most patients with high RSs received chemotherapy (87.0%, 91.1%, and 100% across subgroups), whereas few patients with low scores received it (2.9%, 9.5%, and 26.6% across subgroups). There were no substantial racial/ethnic differences in testing or treatment. Women were largely satisfied with the RS and chemotherapy decisions. **CONCLUSIONS:** Oncologists use the RS to personalize treatment, even for those with node-positive disease. High satisfaction and an absence of disparities in testing and treatment suggest that precision-medicine advances have improved systemic breast cancer treatment. ***Cancer* 2017;123:43-51.** © *2016 American Cancer Society.*

KEYWORDS: adjuvant, breast neoplasms, chemotherapy, genomics, health services, surveys and questionnaires.

INTRODUCTION

A key goal of precision medicine is to reduce treatment burdens in patients with a favorable cancer prognosis. Precision-medicine advances have influenced decisions more strongly for breast cancer than other conditions.[1,2] Until recently, results from cancer staging (particularly the lymph node status) and from tests performed on breast tumors (estrogen receptor [ER], progesterone receptor [PR], human epidermal growth factor 2 [HER2] receptor, and grade) largely determined clinician recommendations regarding adjuvant chemotherapy use in patients with newly diagnosed, early-stage, curable invasive breast cancer.[3,4] In recent years, however, the 21-gene recurrence score (RS) assay, which stratifies a woman's risk for distant breast cancer recurrence into a low, intermediate, or high category and predicts the marginal benefit of adjuvant chemotherapy, has diffused rapidly into clinical practice; it is supported by guidelines on the basis of the strong evidence of its clinical validity and utility.[5-7]

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Current guidelines recommend RS testing for all patients with a favorable prognosis (ER/PR-positive, HER2-negative, node-negative disease) but not for patients with ER/PR-positive, HER2-negative, node-positive disease, for which adjuvant treatment is recommended (independently of RS testing).[3,4] Several studies have shown that RS use for node-negative patients generally follows guideline recommendations with variable evidence of disparities in testing.[8-11] Furthermore, RS results are strongly associated with treatment. RS may reduce the overall use of chemotherapy[12,13] because approximately half of tested patients have low scores that indicate a minimal benefit from chemotherapy, whereas only approximately 10% have high scores that indicate a strong benefit of chemotherapy. Approximately one-third of patients have an intermediate score; in this case, chemotherapy's benefit is less certain.[14] A Canadian study showed that RS testing was followed by a marked increase in the percentage of patients who received a recommendation about chemotherapy (particularly a recommendation against it).[15] However, little is known about how RS results are used by medical oncologists to recommend chemotherapy and whether patients follow these recommendations. Moreover, recommendations and decisions about testing and treatment are less understood in the United States, where RS use is more common and treatment occurs in more diverse settings. Published studies of the RS and treatment decision making have been limited by older diagnosis cohorts, a lack of generalizability, incomplete ascertainment of RS testing and/or chemotherapy treatment, and a lack of granular measures of communication and decision making linked to RS results and treatment.

We used a large, contemporary, diverse, population-based sample of patients recently diagnosed with early-stage breast cancer to examine the relations between RS results, clinician recommendations, chemotherapy receipt, and patient experiences with testing and treatment decision making.

MATERIALS AND METHODS

Sampling and Data Collection

The iCanCare study[16] selected 3880 women aged 20 to 79 years who were diagnosed with early-stage breast cancer and treated in 2013-2014 as captured by rapid reporting systems from the Surveillance, Epidemiology, and End Results (SEER) registries of Georgia and Los Angeles County. African American and Latina women were oversampled in Los Angeles County to ensure the diversity of the sample. We identified cases approximately 2 months after breast surgery treatment. Women with stage III or IV cancer, tumors > 5 cm in size, or more than 3 positive lymph nodes were excluded. Non-Hispanic whites and African Americans younger than 50 years in Los Angeles County were not available for sampling because of an ongoing study in those populations. Modified Dillman techniques[17,18] were used to solicit high patient response rates. Women were invited to participate by mail with an upfront $20 cash incentive. Extensive follow-up was conducted for nonresponders. Materials were sent in English except for women with Spanish surnames, who received materials in both English and Spanish.[19] Among the 3880 identified women, 249 were ineligible because they had a prior breast cancer diagnosis or stage III/IV disease; resided outside the SEER registry area; or were deceased, too ill, or unable to complete a survey in Spanish or English. Another 1053 women did not return surveys or refused to participate. SEER registries collect the RS as part of routine surveillance operations, but there are concerns about completeness. Through an agreement between Genomic Health, Inc, and the National Cancer Institute SEER program, records from the 2 data sets were linked with probabilistic methods, including a manual review and adjudication of potential linked pairs to ensure the highest specificity while simultaneously maximizing sensitivity. The results showed that 97.2% of the patients with a SEER-confirmed RS test were linked to the Genomic Health, Inc, test data set. The SEER registries then provided limited SEER data and RS results for iCanCare participants to the University of Michigan, and these were merged with survey data under institutional review board approval from partnering universities and the state departments of public health of Georgia and California. The RS results were linked to the sample of 2578 women (71% of eligible patients). Our analytic sample consisted of 1527 patients with stage I/II, ER/PR-positive, HER2-negative disease.

Measures

We classified patients into 1 of 3 mutually exclusive clinical categories: lymph node–negative, more favorable disease (age at diagnosis ≥ 50 years and/or tumor grade 1/2); node-negative, less favorable disease (age at diagnosis < 50 years and/or grade 3 disease); and node-positive disease. Age and tumor grade were used to derive subgroups because these variables are prognostic for distance recurrence.[3,20] We examined 3 outcomes: the receipt of RS testing (obtained from Genomic Health, Inc), a medical oncologist's recommendation for adjuvant systemic chemotherapy, and the receipt of chemotherapy (both reported from the patient survey). RS results indicated whether the test was performed or not and

the numeric score (0-100 for tested subjects, with higher values reflecting an increased likelihood of distant metastatic breast cancer recurrence and greater benefit from chemotherapy). Scores were categorized in accordance with current guidelines and laboratory reporting (low, 0-17; intermediate, 18-30; high, 31-100). Surveyed patients reported their medical oncologists' recommendations for adjuvant systemic chemotherapy across 5 responses: strongly against chemotherapy, against chemotherapy, left it up to the patient, for chemotherapy, and strongly for chemotherapy. We categorized these into 3 responses: against chemotherapy, left it up to patient, and for chemotherapy. Women indicated whether they had begun or were planning to begin chemotherapy or whether they had refused or had no plans to begin chemotherapy.

Covariates were obtained from the patient survey and SEER registries. Tumor stage (I or II), grade (1, 2, or 3), and lymph node status (all nodes negative or 1-3 nodes positive for disease) were obtained from registries. Patients provided the following variables from surveys: age at diagnosis; education (high school or less, some college, or college graduate or higher); family income (<$20,000/y, $20-60,000/y, or > $60,000/y); race/ethnicity (white, black, Latina, or Asian); and diagnosis of comorbidities, including chronic lung disease, heart disease, diabetes, or stroke (no diagnosis, 1 condition, or 2 or more conditions).

We also examined patients' experiences with testing and chemotherapy decisions. We first asked tested women how helpful the RS was in making a chemotherapy decision on a 5-point Likert scale (from not at all helpful [1] to extremely helpful [5]). Next, women indicated how the RS affected their interest in chemotherapy: much less interested, less interested, no change in their mind, more interested, or much more interested. We asked women about their satisfaction with decisions surrounding the RS and chemotherapy on a 5-point Likert scale (from not at all satisfied [1] to totally satisfied [5]).

Statistical Analysis

First, we described the association of patient characteristics and the receipt of chemotherapy and RS tests. We then described medical oncologists' recommendations for adjuvant systemic chemotherapy by clinical group and RS score. We then assessed chemotherapy use by clinical and RS groups. Next, we constructed a multivariable logistic regression model that examined the receipt of RS testing as a function of the clinical group, comorbidities, and various demographic characteristics, including race, education, income, and geographical site. Furthermore, we estimated the effect of the RS on the likelihood of chemotherapy receipt while controlling for the clinical group and demographic characteristics listed previously. Finally, we described patients' recall of RS testing and their satisfaction with testing and treatment decision making.

The survey design and nonresponse weights were created to compensate for the differential probability of selection and to adjust for survey nonresponse to report results that resemble the target populations in Los Angeles County and Georgia.[21] To reduce a potential nonresponse bias due to missing data and changes in versions of the questionnaire, we multiply imputed data with a sequential regression multiple imputation framework.[22] We generated 5 independently imputed data sets and then computed inferential statistics; we combined estimates across the data sets.[23] Unless noted, the reported results were based on multiply imputed weighted data (SAS version 9.4).

RESULTS

Table 1 shows the distributions of key variables from observed, unweighted data and the receipt of testing and chemotherapy by the covariate group (unweighted percentages) with corresponding standard errors and *P* values. One-fifth (19.8%) had node-positive disease; 19.4% had node-negative, less favorable disease; and 60.1% had node-negative, more favorable disease. More than one-quarter (27.3%) had 1 or more comorbidities. Patients were widely distributed across race/ethnicity, education, and income categories. Overall, 50.9% of the patients in the analytic sample received an RS: 62.6% of those with node-negative, more favorable disease; 24.3% with node-negative, less favorable disease; and 13.0% with node-positive disease. RS testing was more common in the Georgia cohort versus Los Angeles County cohort (65.8% vs 34.2%, $P < .001$). Overall, 30.9% of the patients received chemotherapy. Few patients in the more favorable group (25.2%) received chemotherapy in comparison with those with less favorable disease (30.3% with less favorable, node-negative disease and 44.3% with node-positive disease). Chemotherapy use was less frequent in older women and those with more comorbidities. Among RS recipients (n = 778), low scores (61.7%) were more common than intermediate (30.0%) or high scores (8.3%).

Factors Associated With RS Testing

Figure 1 shows the results of a logistic regression model that estimates factors associated with RS receipt. Compared with women with node-negative, more favorable disease, women with node-negative, less favorable disease

TABLE 1. Patient Characteristics

Characteristic[a]	No. of Patients	Full Sample (n = 1527)	Received RS Assay (n = 778)	Received Systemic Chemotherapy (n = 472)
Age at diagnosis, mean (95% CI), y		61.0 (60.5-61.6)	59.1 (58.4-59.8)[b]	57.2 (56.2-58.2)[b]
Clinical group, % (SE)				
Lymph node–negative, more favorable disease: age ≥ 50 y or grade 1/2	917	60.1 (1.3)	62.6 (1.7)[c]	25.2 (2.0)[c]
Node-negative, less favorable disease: age < 50 y or grade 3	297	19.4 (1.0)	24.3 (1.5)	30.3 (2.1)
Node-positive disease	303	19.8 (1.0)	13.0 (1.2)	44.3 (2.3)
Missing	10	0.7 (0.2)	0.1 (0.1)	0.2 (0.2)
Comorbidities, % (SE)[d]				
No diagnosis	1102	72.2 (1.2)	74.6 (1.6)[e]	76.1 (2.0)[e]
1 condition	328	21.5 (1.1)	21.0 (1.5)	19.7 (1.8)
2 or more conditions	88	5.8 (0.6)	3.9 (0.7)	3.8 (0.9)
Missing	9	0.6 (0.2)	0.6 (0.3)	0.4 (0.3)
Race/ethnicity, % (SE)				
White	869	56.9 (1.3)	62.0 (1.7)[c]	51.7 (2.3)[b]
Black	233	15.3 (0.9)	15.0 (1.3)	17.2 (1.7)
Latina	268	17.6 (1.0)	13.2 (1.2)	20.3 (1.9)
Asian	112	7.3 (0.7)	6.7 (0.9)	7.2 (1.2)
Missing	45	2.9 (0.4)	3.1 (0.6)	3.6 (0.9)
Education, % (SE)				
High school/GED or less	449	29.4 (1.2)	26.0 (1.6)[c]	28.8 (2.1)
Some college or technical school	491	32.2 (1.2)	31.9 (1.7)	32.2 (2.2)
College graduate or higher	567	37.1 (1.2)	40.9 (1.8)	37.3 (2.2)
Missing	20	1.3 (0.3)	1.3 (0.4)	1.7 (0.6)
Annual family income, % (SE)				
<$20,000	234	15.3 (0.9)	14.7 (1.3)[c]	15.0 (1.7)
$20,000-$60,000	417	27.3 (1.1)	24.8 (1.6)	26.1 (2.0)
>$60,000	583	38.2 (1.2)	43.3 (1.8)	42.2 (2.3)
Missing	293	19.2 (1.0)	17.2 (1.4)	16.7 (1.7)
Site, % (SE)				
Georgia	839	54.9 (1.3)	65.8 (1.7)[c]	51.7 (2.3)
Los Angeles County	688	45.1 (1.3)	34.2 (1.7)	48.3 (2.3)

Abbreviations: CI, confidence interval; GED, general equivalency diploma; RS, recurrence score; SE, standard error.
[a] All percentages are unweighted.
[b] $P < .05$.
[c] $P < .001$.
[d] Patients reported that a physician in the past had told them that they had chronic lung disease, heart disease, diabetes, or a stroke.
[e] $P < .01$.

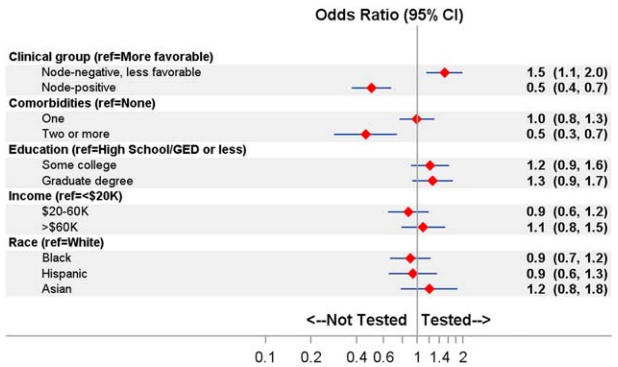

Figure 1. Factors associated with recurrence score testing. Adjusted odds ratios (95% CIs) were estimated with a weighted logistic regression model based on multiply imputed data. They were adjusted for the geographic site. CI indicates confidence interval; GED, general equivalency diploma; K, thousand; ref, reference group.

were more likely to receive an RS (odds ratio [OR], 1.5; 95% confidence interval [CI], 1.1-2.0), whereas women with node-positive disease were less likely to receive an RS (OR, 0.5; 95% CI, 0.4-0.7). Women with 2 or more comorbidities were less likely to receive an RS than women without a comorbidity (OR, 0.5; 95% CI, 0.3-0.7). There were no significant differences in RS use across education, income, and race/ethnicity categories.

Factors Associated With Chemotherapy Recommendations

Overall, 47.2% of the patients reported that their medical oncologist recommended against systemic chemotherapy, 12.3% reported that their oncologist left the decision to them, and 40.5% reported that their oncologist recommended chemotherapy. Figure 2 shows the relationship

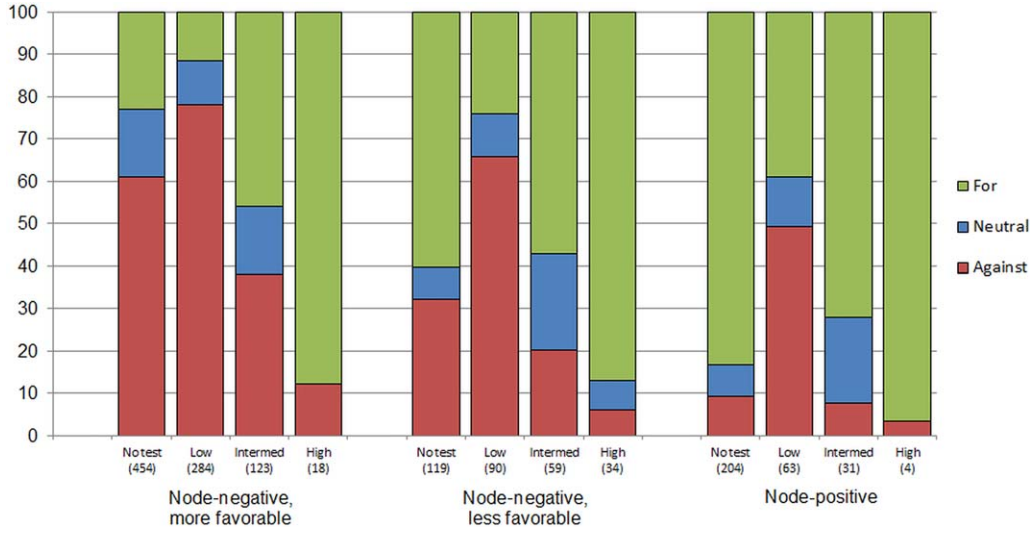

Figure 2. Medical oncologists' recommendations for adjuvant systemic chemotherapy by clinical and recurrence score testing subgroups. The distributions (percentages) of medical oncologists' recommendations for chemotherapy (for, neutral, or against) were estimated from multiply imputed data. The reported sample sizes were weighted and averaged across multiple imputation iterations. Intermed indicates intermediate.

between RS results and medical oncologist recommendations for the 3 clinical groups. RS results were highly associated with recommendations: virtually all patients with high scores (31-100) received a chemotherapy recommendation (86.9%-96.5% across subgroups). For women with node-negative disease, the majority with low-risk RS results (0-18) received a recommendation against chemotherapy (65.9%-78.2% across subgroups). Most women with favorable-risk, node-negative disease received a recommendation against chemotherapy (78.2%), and 11.7% received a recommendation for chemotherapy. Recommendations for chemotherapy varied in untested patients: 23.1% in the more favorable group; 60.2% in the node-negative, less favorable group; and 83.2% in the node-positive group ($P < .001$). Women with less favorable disease and intermediate RS results (19-30) reported the highest proportions of a neutral oncologist recommendation (22.9% and 20.2% of those with node-negative and node-positive disease, respectively).

Factors Associated With Chemotherapy Receipt

Figure 3 shows the distribution of chemotherapy receipt by clinical and RS groups. The relationship between the receipt of chemotherapy and the RS was consistent across the 3 clinical subgroups. Most patients with a high RS received chemotherapy (87.0%, 91.1%, and 100% for the node-negative, more favorable group, the node-negative, less favorable group, and the node-positive group, respectively). Low scores were associated with low rates of chemotherapy in all clinical subgroups (2.9%, 9.5%, and 26.6%, respectively). Intermediate scores yielded rates between the low- and high-score groups. Absolute differences in chemotherapy receipt were particularly marked for patients with a low RS versus patients with no testing. In node-positive disease, 83.2% of untested women received chemotherapy, whereas 27.2% of women with a low RS did. In node-negative favorable disease, 13.0% of untested women received chemotherapy, whereas 3% of women with a low RS did.

Figure 4 shows results of a multivariable logistic regression model examining the association between chemotherapy receipt and selected covariates. The receipt of chemotherapy was associated with clinical subgroups and RS scores. Compared with women who did not have an RS, women with low-risk RS results were less likely to receive chemotherapy (OR, 0.1; 95% CI, 0.1-0.2), whereas women with medium- and high-risk RS results were more likely to receive chemotherapy (OR for medium-risk results, 1.4; 95% CI, 1.1-1.7; OR for high-risk results, 2.8; 95% CI, 2.0-4.0). Compared with women with more favorable node-negative disease, women with node-negative disease but 1 unfavorable risk factor were more likely to receive chemotherapy (OR, 4.4; 95% CI, 3.1-6.2), whereas women with node-positive disease were considerably more likely to receive chemotherapy (OR, 18.9; 95% CI, 13.0-28.0). Higher income patients were more likely to receive chemotherapy than lower income patients (OR, 1.6; 95% CI, 1.0-2.4), but there were no differences in receipt by education or race/ethnicity. To investigate

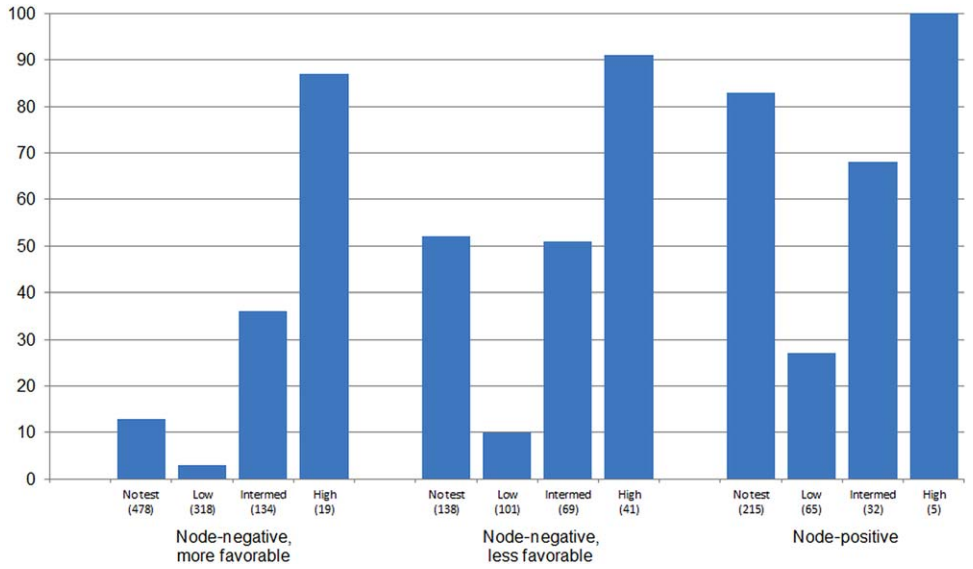

Figure 3. Receipt of adjuvant systemic chemotherapy by clinical and recurrence score testing subgroups. The sample sizes below each bar were weighted and averaged across multiply imputed data sets by subgroup. Intermed indicates intermediate.

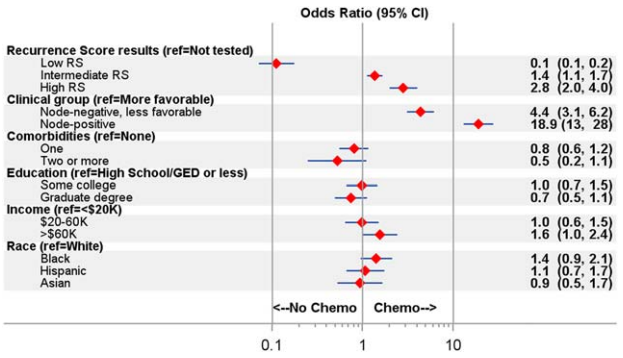

Figure 4. Factors associated with the receipt of adjuvant systemic chemotherapy. Adjusted odds ratios (95% CIs) were estimated with a weighted logistic regression model based on multiply imputed data. They were adjusted for the geographic site. Chemo indicates receipt of adjuvant systemic chemotherapy; CI, confidence interval; GED, general equivalency diploma; K, thousand; ref, reference group.

differences by race/ethnicity, we examined chemotherapy receipt by clinical subgroup, RS status, and race/ethnicity (full results not shown). The only subgroup in which white women had notably higher rates of chemotherapy receipt than other racial/ethnic groups was the node-positive disease group with an intermediate RS (79% of whites, 50% of Asian women and Latinas, and 20% of black women).

Patient Experiences With Testing and Chemotherapy Decisions

We compared observed self-reported RS results with RS test results from Genomic Health, Inc. Approximately three-quarters of the patients (76.5%) accurately reported RS receipt, and among those who did receive an RS, 61.7% correctly reported the results by category (low, intermediate, or high risk). Among those who received an RS, 63.9% reported that it was "very" or "extremely" helpful. Among the 420 women who reported low-risk RS results, 65.0% indicated that the RS shifted their opinion against chemotherapy, whereas 73.1% of those who reported high scores reported that their RS result shifted their opinion toward the receipt of chemotherapy. Satisfaction with decision making about RS testing and the receipt of chemotherapy was very high (4.4 of 5.0 for both decisions), and these scores did not differ substantively whether patients did or did not receive testing or chemotherapy.

DISCUSSION

We examined patient experiences with RS and chemotherapy use in a diverse, contemporary, population-based sample of breast cancer patients. RS use closely followed practice guidelines. A majority of patients with node-negative disease received an RS, but fewer node-negative patients with less favorable characteristics (younger age or higher grade) received an RS; this may reflect clinicians' planned chemotherapy use for these higher risk patients, which thus negated the need for RS testing. Substantial RS use for node-positive patients underscores clinicians' growing support of wider RS use for tailoring treatment recommendations despite guidelines recommending

chemotherapy (and no RS testing) for these patients. These results suggest that clinicians find the RS useful when chemotherapy is less clearly indicated. Results from the RxPONDER trial will clarify the clinical utility of testing in patients with node-positive disease.[24] The utility of the RS in women with tumors < 0.5 cm and without adverse features remains unclear.[1]

RS results correlated strongly with clinician recommendations and the receipt of chemotherapy; chemotherapy was recommended for virtually all patients with high scores but was discouraged for most patients with low scores. The RS effect appeared greatest with less favorable disease. Importantly, we observed no marked educational or racial/ethnic gradient in RS testing or treatment. Patient recall of RS results was moderate (60% accuracy), and this suggests that many patients deferred the integration of RS results to the physician. This also suggests an opportunity for targeted educational interventions to improve patient understanding of RS results and their role in patient decision making. Finally, patients were highly satisfied with the RS testing and treatment decision-making process.

Our findings add to prior studies that have examined RS use and treatment in breast cancer. In an Ontario study conducted between 2012 and 2013, patients and physicians completed surveys before and after RS testing.[15] After RS results were shared, oncologists changed their initial recommendation 51% of the time, and this resulted in lower chemotherapy use. Patients' decisional uncertainty was reduced after RS testing. Our study findings support low decision uncertainty in a diverse patient population with access to RS testing in the United States. In a North Carolina study of women diagnosed with breast cancer between 2008 and 2013, approximately 40% of patients received RS, with similar rates between node-positive and node-negative patients[9]; however, RS testing was ascertained by pathology reports alone, which may be prone to missing information.[25] Our study suggests substantial RS testing and a clinical impact for patients with node-positive disease. Although investigators have documented high patient and clinician satisfaction with RS testing,[26] others have noted substantial variations in the chemotherapy decision-making process.[27] Potosky et al[10] showed that RS results were highly associated with chemotherapy use in a cohort that was treated before 2012 and found no socioeconomic disparities; however, few nonwhite patients were studied. Our study confirms the absence of socioeconomic testing differences in a large, diverse, population-based sample. A recent study suggested less than optimal adherence to guidelines with respect to testing and treatment.[28] Our study suggests robust uptake of RS testing in guideline-concordant clinical subgroups and provides insight into reasons for testing patterns.

Aspects of our study merit comment. Strengths include a large, contemporary, diverse, population-based sample; a high response rate; valid measures of RS testing (including actual results obtained from the laboratory); clinical and treatment variables; and granular measures of patient experiences and appraisal of testing and treatment. Our analytic techniques reduced the potential nonresponse bias and account for missing data. However, our results are limited to 2 large geographic regions of the United States. Measures of communication and decision making were ascertained through patients and do not necessarily represent physician perspectives.

Implications

Our results suggest that a major advance in oncology precision medicine, tumor genomic profiling, may improve treatment decision making and communication. In the context of early-stage breast cancer, the combination of genomic test results and clinical data now offers more precise targeting of patients for chemotherapy, especially among those with node-negative disease. Additional clarity about the prediction of the marginal benefit of adjuvant chemotherapy for node-negative disease patients with an intermediate score is forthcoming.[29]

The majority of the studied patients reported that their medical oncologist made a recommendation for or against chemotherapy rather than leaving the decision to the patient. Personalized recommendations appear to reduce potential overtreatment with chemotherapy and nearly eliminated socioeconomic disparities in treatment after we controlled for clinical factors. This is a notable benefit of incorporating the RS into breast cancer treatment algorithms. Oncologists' commitment to addressing overtreatment may be most evident in the substantial proportion of patients with node-positive disease who received an RS despite current guidelines that advise chemotherapy without RS testing. The impact of RS testing appeared greatest for node-positive patients because their baseline use of chemotherapy was high: RS results largely served to identify node-positive patients with low scores for whom chemotherapy might logically be omitted. However, definitive evidence for the benefit of RS testing among node-positive patients awaits the results of clinical trials.[24] Finally, our results suggest that many patients rely on their oncologist to incorporate RS results into chemotherapy recommendations and that patient

satisfaction with RS testing and treatment decisions is very high. This underscores another potential impact of precision medicine: reducing lingering uncertainty and improving the patient experience with treatment decision making and communication.

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CONFLICT OF INTEREST DISCLOSURES

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AUTHOR CONTRIBUTIONS

Christopher R. Friese: Conceptualization, methodology, investigation, writing–original draft, writing–review and editing, and visualization. Yun Li: Methodology, investigation, software, formal analysis, writing–original draft, and writing–review and editing. Irina Bondarenko: Methodology, investigation, software, formal analysis, writing–original draft, writing–review and editing, and visualization. Timothy P. Hofer: Methodology, investigation, formal analysis, writing–original draft, and writing–review and editing. Kevin C. Ward: Conceptualization, methodology, investigation, writing–original draft, and writing–review and editing. Ann S. Hamilton: Conceptualization, methodology, investigation, writing–original draft, and writing–review and editing. Dennis Deapen: Conceptualization, methodology, investigation, writing–original draft, and writing–review and editing. Allison W. Kurian: Conceptualization, methodology, investigation, writing–original draft, and writing–review and editing. Steven J. Katz: Conceptualization, methodology, investigation, writing–original draft, writing–review and editing, and visualization.

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