Original Study

Clinical Impact of 21-Gene Recurrence Score Test Within the Veterans Health Administration: Utilization and Receipt of Guideline-Concordant Care

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Abstract

As more veterans seek breast cancer care within the Department of Veterans Affairs, we evaluated whether node-negative, hormone receptor–positive patients received 21-gene Recurrence Score testing to predict breast cancer recurrence. Analysis of 2011-2012 Veterans Affairs Central Cancer Registry, chart, and laboratory data revealed that 82 (25%) of 328 eligible veterans underwent the test. Most of the tested patients received guideline-concordant care.

Introduction: Ensuring guideline-concordant cancer care is a Department of Veterans Affairs (VA) priority, especially as the number of breast cancer patients at VA medical centers (VAMCs) grows. We assessed the utilization and clinical impact of the 21-gene Recurrence Score test, which predicts 10-year risk of breast cancer recurrence and the likelihood of chemotherapy benefit, on veterans newly diagnosed with breast cancer. **Patients and Methods:** We conducted a retrospective cohort study using 2011-2012 VA Central Cancer Registry, chart review, and laboratory test data. Independent variables assessed included patient and site-of-care characteristics. The outcome of interest was whether newly diagnosed, eligible (node negative, hormone-receptor positive, human epidermal growth factor receptor 2 [*HER2*] negative) veterans underwent the 21-gene test. We performed descriptive statistics on all patients and multivariate logistic regression to determine associations. We correlated treatments received with test results. **Results:** Among 328 eligible veterans, 82 (25%) had the 21-gene test; 100 eligible veterans (30%) sought care at a VAMC where no tests were ordered. Receiving care at a VAMC that had women's health services (odds ratio [OR], 1.84, 95% confidence interval [CI], 1.05-3.22) and having tumor characteristics meeting the National Comprehensive Cancer Network 2010 test criteria (OR, 3.06, 95% CI, 1.69-5.57) were positive predictors of testing; increasing age (OR, 0.93, 95% CI, 0.91-0.96 per year) and fee-based care (OR, 0.46, 95% CI, 0.26-0.82) were negative predictors. The majority of tested patients received guideline-concordant care. **Conclusion:** Site of care and tumor characteristics were important predictors of test uptake. Facilitating delivery of guideline-concordant cancer care requires improved laboratory informatics and clinical decision support.

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Introduction

Female veterans are the most rapidly growing patient population within the Department of Veterans Affairs (VA).[1] Given the expansion of this population, improving access to women's health services, including breast cancer screening and appropriate treatment, are strategic priorities of the VA.[2] The VA recognized that the

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number of breast cancer cases was rising,[3,4] and in 2010 it expanded its capacity to offer breast cancer treatment within VA medical centers (VAMCs). Evaluating use of guideline-concordant care among breast cancer patients is necessary to ensure quality of care, especially given that the number of breast cancer cases treated per VAMC is still relatively small.[4]

An important component of breast cancer care is risk stratification, which is performed in order to identify appropriate therapies while minimizing exposure to unnecessary and potentially harmful adverse effects. The 21-gene Recurrence Score assay (Oncotype DX Breast Cancer Assay), developed and conducted by Genomic Health (Redwood City, CA), is a diagnostic test that estimates the likelihood of 10-year recurrence in early-stage, hormone receptor (HR)-positive breast cancer.[5] Tumors are categorized as having a low-risk score ($\leq$ 18 points), moderate-risk score (18-30 points), or high-risk score ($>$ 30 points), with an average 10-year recurrence risk of 7%, 14%, and 31%, respectively.[5]

Since 2008, the 21-gene test has been recommended for breast cancer patients diagnosed with estrogen receptor−positive, lymph node (LN)-negative disease by the American Society of Clinical Oncology (ASCO) and the National Comprehensive Cancer Network (NCCN).[6,7] While the ASCO guidelines were less stringent, stating that the 21-gene test assay could be used in newly diagnosed patients with node-negative, estrogen receptor−positive disease,[7] the NCCN guidelines further restricted recommendations for testing to individuals with tumor size of 0.6 to 1.0 cm with grade II or III histology, or tumor $>$ 1 cm (any grade).[6] Among those with low risk scores, hormone therapy alone can be used with freedom from recurrence of $>$ 98% at 5 years.[8] Among those with high risk scores, adjuvant chemotherapy in addition to hormone therapy showed improvements in disease-free survival.[9] The value of adjuvant chemotherapy is unclear in intermediate-risk patients.[6]

Although the 21-gene test was initially developed and validated in female breast cancer patients, male and female breast cancers have similar pathology, including a predominance of estrogen and progesterone receptor−positive cancers in both sexes as well as identical staging. Additionally, treatment for male breast cancer is based on treatment of female breast cancers, given the lack of randomized trial data for male breast cancer.[10,11] Finally, the ASCO and NCCN guidelines for management of early-stage invasive breast cancer do not discriminate by sex.[6,7]

Several studies have examined the cost-effectiveness and clinical utility of the 21-gene test.[12,13] Utilization has more recently been examined; among Medicare beneficiaries with newly diagnosed breast cancer from 2010 to 2013, only 9.9% were found to have a claim for this test, although the study did not account for tumor characteristics and thus could not identify test-eligible patients; the authors estimate that among LN−, HR^+, human epidermal growth factor receptor 2 (*HER2*)-negative Medicare patients, at least 31% had testing.[14]

Given the growing emphasis on women's health initiatives and incorporating genomic medicine in the VA, we evaluated utilization of the 21-gene test among eligible veterans diagnosed with breast cancer between 2011 and 2012. We sought to identify both patient and site-of-care characteristics associated with test utilization. Finally, we assessed the use of hormone therapy and adjuvant chemotherapy among eligible patients by 21-gene test status.

Patients and Methods

Study Population

We conducted a retrospective cohort study using secondary data analysis methods. The primary sources of data were the VA Central Cancer Registry,[15] a database that contains information on cancer diagnosis and treatment at each of the 132 VAMCs that diagnose and/or treat veterans with cancer, the VA's electronic medical record, Computerized Patient Record System, the VA's Corporate Data Warehouse, the VA Support Service Center, and patient-level laboratory test data obtained from Genomic Health. We obtained permission to conduct this research from both the Bedford and Salt Lake City VA institutional review boards and research and development committees, which authorized a waiver of both informed consent and Health Insurance Portability and Accountability Act authorization.

Using the VA Central Cancer Registry, we identified 1082 patients diagnosed with breast cancer between January 1, 2011, and December 31, 2012, as well as their LN, HR, and *HER2* status. Patients were defined as eligible for 21-gene testing if they were LN−, HR^+, and *HER2*−, which was based on a patient's *HER2* summary status. Patients not meeting these criteria were considered ineligible for 21-gene testing in this study, although a small portion of these patients did indeed undergo testing (n = 35). Our final study population included 328 test-eligible breast cancer patients (Figure 1); very few eligible patients declined 21-gene testing or chemotherapy.

Ascertainment of Patients Receiving 21-Gene Testing

The outcome was a dichotomous variable indicating whether test-eligible patients underwent the 21-gene test. We used a 3-pronged approach to identify whether this occurred. First, we used data provided by Genomic Health, which included patient name, medical record number, and place of care, to link 21-gene test orders to the VA Central Cancer Registry data. Next, we conducted a keyword search of the electronic health records of newly diagnosed breast cancer patients using the terms "recurrence score," "oncotype," "genomic health," "risk score," "21-gene," and "gene expression." Finally, we conducted manual chart review to identify whether there were patients who declined a 21-gene test or who were tested outside the VA. Patients who declined testing or who had an indication of testing outside the VA were identified as tested (Figure 1). However these patients lacked test result information.

Predictor Assessment

We evaluated patient and site-of-care characteristics associated with testing. We obtained patient-level characteristics from the VA Central Cancer Registry and Corporate Data Warehouse, including age, race, year of diagnosis, and fee-based care. We also assessed tumor characteristics among eligible patients, including tumor size and grade, and created a dichotomous variable, "NCCN Criteria Met," which identified a subgroup of patients with tumor size 0.6 to 1.0 cm and grade II or III histology, or tumor size $>$ 1 cm (Table 1). We assessed site-of-care characteristics using the VA Support Service Center and Site Tracking Database, including the following: Commission on Cancer accreditation status, existence of a women's health service clinic, and distance from a National