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Utilization of genetic testing in breast cancer treatment after implementation of comprehensive multi-disciplinary care

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Abstract

To evaluate the utilization of genetic testing after implementing a comprehensive multi-disciplinary care (cMDC) program for breast cancer and to assess for racial disparities. This retrospective study included patients newly diagnosed with invasive breast cancer 1 year before and 1 year after implementing a cMDC program to assess the rate of genetic referrals. Appropriate genetic referrals were defined by age, family history, triple-negative status, and personal history based on National Comprehensive Cancer Network guidelines. Secondary outcomes included rates of recommended testing, actual testing, compliance, and equity in genetic referrals across demographics (race, insurance type, and hospital site). Statistical analyses used the Fisher exact test or chi-square test. The 431 patients identified included 116 non-cMDC and 315 cMDC patients. Following implementation of cMDC, a significant increase occurred not only in appropriate genetic referrals (35.3%-55.5%) but also in inappropriate referrals (1.7%-15.5%) ($P = .001$). Overall attendance increased among both cohorts, Caucasians were more compliant with attending their genetic appointment compared to their African American counterparts (non-cMDC $P = .025$, cMDC $P = .004$). In the cMDC group, African Americans demonstrated a 6% increase in attendance compared to a 2% decrease among Caucasians. More appropriate genetic referrals were made to those with private insurance following implementation of cMDC. Utilizing a cMDC approach to breast cancer care may help increase appropriate utilization of genetics.

Keywords

compliance; genetic testing; multi-disciplinary cancer care program; racial disparities

1 | INTRODUCTION

Historically, surgery was the primary method for treating breast cancer.¹ More recently, the diagnosis and treatment of breast malignancies have escalated in their sophistication and complexity.^{2,3} With the advent of screening mammography, hormonal therapy, chemotherapy, and breast-conservation treatment, medical and radiation oncologists now have major roles in curative treatment. Therefore, the direction of breast cancer care has

moved toward a multifaceted approach with the involvement of many disciplines of medicine, both diagnostic and therapeutic.⁴⁻⁶

One key player in the multi-disciplinary breast tumor board should be the geneticist as genetic screening is an integral part of breast cancer treatment.⁷⁻¹⁰ The identification of the BRCA gene offers an unprecedented opportunity for high-risk members of families with hereditary breast-ovarian cancer to learn whether they carry a cancer-predisposing mutation.¹¹ Women found to carry a BRCA mutation have up to an 85% lifetime risk of breast cancer, a 20%-65% lifetime risk of ovarian cancer, and an increased risk of colon cancer.¹² Men who carry the BRCA mutation are at increased risk for prostate and colon cancer and can also transmit the gene mutation to their daughters. Early identification of BRCA mutation carriers within hereditary breast-ovarian cancer families can allow for targeted surveillance and management strategies.^{13,14}

Fewer than 1 in 5 individuals with breast cancer who meet National Comprehensive Cancer Network (NCCN) criteria have undergone genetic testing.¹⁵ Rates of appropriate referrals for genetic testing have been reported to be higher in a multi-disciplinary setting.¹⁶ Evidence also suggests that racial disparities exist with genetic referrals in patients with cancer.^{17,18} Our academic health system in southeast Michigan recently adopted a comprehensive and structured multi-disciplinary care approach to breast cancer treatment, including the participation of a geneticist. This study aimed to evaluate the appropriate referral and use of genetic testing after implementing a comprehensive multi-disciplinary care (cMDC) program and to assess for differences by race, location of care, and insurance status.

2 | MATERIALS AND METHODS

This retrospective study was approved with waiver of consent by the health system's institutional review board. We used the electronic medical record system to identify all patients from February 2015 to February 2017 with newly diagnosed invasive breast cancer who were treated at two of the health system sites, one suburban and one urban location. The cMDC program at both sites involved the same staff but was held on different days of the week. Patients who received treatment at outside institutions or other locations of our health system were excluded. The primary outcome was to assess the impact of the cMDC program on appropriate genetic referral, and secondary outcomes were to assess any differences between the two sites of care, insurance status, and race in appropriate utilization of genetic services.

Patients were categorized as non-cMDC (February 2015 to January 2016) and cMDC (February 2016 to February 2017). Data obtained from chart review included age, race, parity, county of residence, gender, and type of insurance (private vs public). Patients who had Medicare and private insurance were categorized as having private insurance. Genetic testing referrals were categorized as appropriate based on NCCN guidelines¹⁹:

1. early age onset breast cancer
2. two breast primaries or breast and ovarian cancer in a single individual

3. Two or more breast primaries or breast and ovarian cancers in close relatives from the same side of family
4. clustering of breast cancer with one or more of the following: thyroid cancer, sarcoma, adrenocortical carcinoma, endometrial cancer, pancreatic cancer, brain tumors, dermatologic manifestations or leukemia/lymphoma on the same side of the family
5. member of a family with a known mutation in a breast cancer susceptibility gene
6. population at risk ie women of Ashkenazi Jewish descent with breast or ovarian cancer at any age
7. any male breast cancer
8. ovarian cancer on the same side of family.

The geneticist was present at all tumor board discussions. When a patient met the NCCN criteria, a referral to the geneticist was placed, and the patient was scheduled to meet with a genetic counselor the same day after tumor board.

2.1 | Statistical analysis

Sample size calculation, using a power of 0.80, national rate of appropriate genetic referral rate of 20% and a type I error rate of 5%, determined a sample size of 246 was needed for an adequately powered study. Statistical analyses used Fisher exact test in the presence of sparse categories (ie, expected cell counts <5) or chi-square test. All analyses were done with SPSS Statistics (IBM), with significance set at $P < .05$.

3 | RESULTS

The 431 patients identified included 116 (26.9%) non-cMDC and 315 (73.1%) cMDC patients (Table 1). The average age was 61 years, and 43.4% were African American (AA) and 56.4% Caucasian (CA). More patients had private insurance (65.7%) than public insurance (33.9%). The cMDC and non-cMDC groups were similar in demographics, except more patients were seen at the urban location. The overall rate of genetic referrals was higher after implementation of cMDC (37%-71%, $P = .001$). However, the cMDC group also demonstrated a higher rate of inappropriate referrals (15.5% vs 1.7%, $P = .001$) (Table 1).

Genetic referral overall increased for both races following implementation of cMDC (35.7%-67.2% AA, $P = .001$, and 38.3%-73.8% CA, $P = .001$). Within each cohort, AA and CA patients were offered genetic appointments at similar rates (Table 2). Overall, AA patients were less likely to comply with attending the genetics appointment (86% AA vs 98% CA for cMDC, $P = .004$, and 80% AA vs 100% CA for non-cMDC, $P = .025$; Table 2). When patients attended the genetics appointment, genetic testing was recommended at similar rates for AA and CA patients (Table 2). For those whom testing was recommended, rates of actual testing were similar for both races (91% vs 92% non-cMDC, $P = .968$, and 98% vs 100% cMDC, $P = .337$).

In the cMDC group, appropriate genetic referrals were slightly higher at the suburban than the urban location, but not statistically significant (60.7% vs 50.9%, $P = .082$; Table 3). Inappropriate referrals were offered similarly at both locations. Significantly more cMDC patients attended their appointment at the suburban location vs the urban location (97.6% vs 89.3%, $P = .047$). Genetic testing was recommended at similar rates at both locations (Table 3). For those whom testing was recommended, rates of actual testing were similar across locations (90.5% vs 93%, $P = .802$, and 98% vs 100%, $P = .242$).

Genetic referral was offered (both appropriately and inappropriately) more often in cMDC patients with private than public insurance (76.7% vs 60.8%, $P = .003$; Table 4). Although inappropriate genetic referrals were made similarly in both cohorts, more patients with private insurance received appropriate referrals than those with public insurance (61.2% vs 44.9%, $P = .006$). Genetic appointments were attended at similar rates, and genetic testing was recommended at similar rates across cohorts (Table 4). For those whom testing was recommended, rates of actual testing were similar across insurance types (100% vs 88%, $P = .251$, and 100% vs 97%, $P = .303$).

Overall, once referred, genetic testing was recommended or offered at a rate of 88.8% and performed at a rate of 95.8%. No statistical difference was found between study groups.

4 | DISCUSSION

This study showed a significant increase in genetic referrals as well as scheduled and attended genetic appointments following implementation of cMDC for patients with invasive breast cancer at our institution. This may be attributed to scheduling an appointment at the time of tumor board instead of addressing it at a later time. Our study findings are consistent with the literature that indicates genetic referrals have been underutilized for eligible women based on NCCN guidelines.^{20,21}

The literature also suggests that a lower proportion of AA women undergo genetic testing raising concerns about racial disparities in genetic counseling and testing.^{22,23} The overall rate of genetic referral increased with the implementation of cMDC and did not disproportionately increase based on race. However, AA women were less likely to attend their genetic appointments. Among the women who did attend their appointments, there was no difference in the rates of genetic testing recommended or completed, suggesting that the barrier to testing most likely lies in the adherence to genetic appointments in this cohort.

Although genetic referrals increased following the implementation of cMDC, the rates of genetic testing recommended and subsequently performed by the geneticist were similar between the study groups. This suggests that lack of referral for eligible patients in the non-cMDC group may have been the limiting factor for receipt of the service, as genetic services were provided once referred. The number of inappropriate referrals also increased with the implementation of cMDC, which indicates providers may require reminders or education about NCCN criteria, especially as inappropriate referral may be associated with unnecessary health care costs. A cost-benefit analysis was not a goal of this study, but this

finding highlights the need for providers to adhere to NCCN guidelines for genetic referral in the management of patients diagnosed with invasive breast disease.

While genetic appointments were offered significantly more at both the urban and suburban location following the implementation of cMDC, genetic appointments were attended more often at the suburban location. Several factors have been associated with offering genetic referral, including college education, age below 45 years, household income >\$35 000 in the year prior to diagnosis, and private health insurance.²⁴⁻²⁶ In our study, genetic referrals were more likely to be offered to patients with private insurance. An association between location of facility and genetic referral has not been previously reported, and future studies are needed to evaluate the observed difference in this study population.

Limitations of this study include its retrospective design, and thus, findings can only be associated with, not causative of, implementation of cMDC. Our study population may not be generalizable to other groups across the United States.

5 | CONCLUSION

Implementation of a cMDC approach to invasive breast cancer care at our academic health system significantly improved rates of appropriate patient referral to and patient use of genetic services regardless of race, location of care, or type of insurance. As a testament to the overall success of the program, referral to genetic screening services improved to 71% following implementation and subsequent genetic testing was recommended or offered at an astounding rate of 88.8% and performed at a rate of 95.8%, compared to the 20% national rate of genetic testing. While no differences were found between AA and CA patients in referral to genetic services or in recommendation for genetic testing, more AAs did not attend their genetic appointment compared to CAs both before and after implementation of cMDC. This suggests more effort is needed to identify reasons for missed appointments to overcome this disparity. However, we must note that there was an overall high rate (>80%) of genetic appointment attendance in both cohorts. Our study also suggests that providers may require reminders or education to follow the NCCN guidelines as inappropriate referrals for genetic services significantly increased after cMDC implementation.

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TABLE 1

Patient demographics and overall summarization

	Total (N = 431)	cMDC (N = 315)	Non-cMDC (N = 116)	P-value
Age (mean ± SD), years	61.7 ± 13.3	62.2 ± 13.5	60.0 ± 12.4	.109(T)
Race				
Caucasian	243 (56.4%)	183 (58.3%)	60 (51.7%)	.287(C)
African American	187 (43.4%)	131 (41.7%)	56 (48.3%)	
Insurance				
Public	146 (33.9%)	107 (34.2%)	39 (33.6%)	.627(C)
Private	283 (65.7%)	206 (65.8%)	77 (66.4%)	
Site				
Urban	245 (56.8%)	165 (52.4%)	80 (69.0%)	.002(C)*
Suburban	186 (43.2%)	150 (47.7%)	36 (31.0%)	
Genetic offered				
Appropriately	216 (50.1%)	175 (55.5%)	41 (35.3%)	.001(C)*
Inappropriately	51 (11.8%)	49 (15.5%)	2 (1.7%)	
No	164 (38.1%)	91 (28.9%)	73 (63%)	
	Total (N = 160)	cMDC (N = 128)	Non-cMDC (N = 32)	P-value
Genetic testing result				
Positive	12 (7.5%)	9 (7.0%)	3 (9.4%)	.231(C)
Negative	118 (73.8%)	91 (71.0%)	27 (84.4%)	
Equivocal	25 (15.6%)	23 (18.0%)	2 (6.2%)	
Declined	5 (3.1%)	5 (4.0%)	0	

Note: Equivocal test results were those that were inconclusive tests with variance of unknown significance.

Abbreviations: C, chi-square test; cMDC, comprehensive multi-disciplinary care; F, Fisher exact test; T, two-sample t test.

* P-value < .05 significant.

TABLE 2

Genetic services by cohort stratified by race

	cMDC			Non-cMDC		
	AA (%)	Caucasian (%)	P-value	AA (%)	Caucasian (%)	P-value
Genetic referral						
Yes, appropriate	50.4	59.6	.268(C)	35.7	35	.386(C)
Yes, inappropriate	16.8	14.2		0	3	
No	32.8	26.2		64.3	61.7	
Genetic appointment attended						
Yes	86	98	.004(F)*	80	100	.025(F)*
No	14	2		20	0	
Genetic testing recommended						
Yes	85.4	88.2	.609(F)	100	92	1.000(F)
No	14.6	11.8		0	8	
Genetic testing completed						
Yes	100	98	.337(F)	100	92	.968(F)
Genetic testing result						
Positive	11	7.9	.584(C)	5.3	15.4	.331(C)
Negative	72.7	67.1		84.2	84.6	
Equivocal	14.5	19.7		10.5	0	
Declined	1.8	5.3				

Note: Percentage of genetic referral received is of total population offered.

Abbreviations: AA, African American; C, chi-square test; cMDC, comprehensive multi-disciplinary care; F, Fisher exact test.

* $P < .05$ significant.

TABLE 3

Genetic services by cohort stratified by location of care

	cMDC		Non-cMDC		P-value	P-value
	Urban (%)	Suburban (%)	Urban (%)	Suburban (%)		
Genetic referral						
Yes, appropriate	50.9	60.7	33.8	38.9	.067(C)	.706(C)
Yes, inappropriate	14.5	16.6	1.2	2.8		
No	34.5	22.7	65	58.3		
Genetic appointment attended						
Yes	89.3	97.6	87.5*	100	.047(F)*	.283(F)
No	10.7	2.4	12.5	0		
Genetic testing recommended						
Yes	84.8	89.4	95.5	93.3	.463(F)	1.000(F)
No	15.2	10.6	4.5	6.7		
Genetic testing completed						
Yes	98	100	90.5	93	.242(F)	.802(F)
Genetic testing result						
Positive	11	7.9	5.3	15.4	.584(C)	.331(C)
Negative	72.7	67.1	84.2	84.6		
Equivocal	14.5	19.7	10.5	0		
Declined	1.8	5.3				

Note: Percentage of genetic referral received is of total population offered.

Abbreviations: C, chi-square test; cMDC, comprehensive multi-disciplinary care; F, Fischer exact test.

* $P < .05$ significant.

Services provided within cMDC group and Non-cMDC group stratified by private and public insurance status

TABLE 4

	cMDC		Non-cMDC		P-value
	Public (%)	Private (%)	Public (%)	Private (%)	
Genetic referral					
Yes, appropriate	44.9	61.2	28.2	39	.482(C)
Yes, inappropriate	15.9	15.5	2.6	1.3	
No	39.2	23.3	69.2	59.7	
Genetic appointment attended					
Yes	97.6	92.4	90.9	92.6	.457(F)
No	2.4	7.6	9.1	7.4	
Genetic testing recommended					
Yes	81	90	91.7	96.2	.512(F)
No	19	10	8.3	3.8	
Genetic testing completed					
Yes	100	97	100	88	.251(F)
Genetic testing result					
Positive	8.6	8.4	0	13.6	.418(C)
Negative	65.7	71.6	90	81.8	
Equivocal	17.1	18	10	4.6	
Declined	8.6	2			

Note: Percentage of genetic referral received is of total population offered.

Abbreviations: C, chi-square test; cMDC, comprehensive multi-disciplinary care; F, Fisher exact test.

* P-value < .05 significant.