Genetic Testing for Breast Cancer Susceptibility Should Be Offered before Unilateral Abdominally Based Free Flap Breast Reconstruction

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Background: Pathogenic mutations have been identified in approximately 10 percent of patients who present with breast cancer. Notably, failure to identify deleterious genetic mutations has particular implications for patients undergoing abdominally based breast reconstruction, as the donor site can be used only once. The authors sought to determine: (1) how many patients underwent genetic testing before unilateral abdominally based free flap breast reconstruction; (2) how often deleterious mutations were detected after abdominally based free flap breast reconstruction; and (3) the cost-effectiveness of expanding genetic testing in this patient population.
Methods: The authors retrospectively identified all patients who underwent unilateral abdominally based free flap breast reconstruction at Brigham and Women's Hospital/Dana-Farber Cancer Institute between 2007 and 2016. Chart review was performed to collect relevant demographic and clinical data. Relevant hospital financial data were obtained.
Results: Of the 713 who underwent free flap breast reconstruction, 160 patients met inclusion criteria, and mean follow-up was 5.8 years. Three patients (1.9 percent of 160) underwent contralateral surgery after completing reconstruction, two of whom had *BRCA2* and one with *ATM* mutation. One hundred eleven patients met National Comprehensive Cancer Network guidelines for genetic testing, but of those only 55.9 percent (62 patients) were tested. Financial data revealed that testing every patient in the cohort would result in a net savings of $262,000.
Conclusions: During a relatively short follow-up period, a small percentage of patients were diagnosed with pathogenic mutations and underwent contralateral mastectomy and reconstruction. However, because of the costliness of surgery and the decreased cost of genetic testing, it is cost-effective to test every patient before unilateral abdominally based free flap breast reconstruction. (*Plast. Reconstr. Surg.* 144: 12, 2019.)

Since *BRCA1/2* mutations were identified in the early 1990s, the concept of prophylactic breast and ovarian surgery in cases of deleterious mutation has been accepted to help prevent breast and ovarian cancer.[1–7] It is known that women with *BRCA1* or *BRCA2* mutations have a risk of breast cancer approximately five times (70 to 80 percent) baseline, and the risk of ovarian cancer is increased 10- to 30-fold.[6,8,9] The impact of genetic mutations on medical decision making may be profound;

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Lokich et al. demonstrated that over 70 percent of patients found to harbor *BRCA* mutations choose surgery different from that initially planned.[6,8–12] Failure to diagnose pathogenic mutations puts individuals at risk for future breast and ovarian cancers, and also has implications for family members.[9,13,14]

Whereas testing was originally offered for *BRCA1/2* only, now extended panels are performed that include additional genes such as *ATM1*, *CHEK2*, and *BRIP1* among others.[15,16] A mutation can be classified as either (1) normovariant or benign, (2) pathogenic or deleterious, or (3) a variant of uncertain significance.[17] A variant of uncertain significance may later be reclassified as benign or pathogenic, and patients may be notified of such a change.[8,9,13,18] Using expanded panel testing, a recent study at our institution showed that 10.7 percent of patients with stage I to III breast cancer were found to harbor pathogenic mutations.[1]

Stratification of breast cancer patients into low-risk and high-risk groups for genetic mutations according to clinical and family histories is now the standard of care.[2,19,20] Guidelines for patient screening are published by the National Comprehensive Cancer Network, and others.[7,21–24] Unfortunately, not all potential carriers are identified by existing criteria for *BRCA* testing.[8,18,25] In fact, 80 percent of the mutation carriers younger than 50 years do not have usual characteristics associated with *BRCA* mutation carriers (i.e., personal/family history of breast and/or ovarian cancer or Ashkenazi Jewish ancestry).[15,23,24,26,27] Because guidelines for testing are imperfect, some women with breast cancer and pathogenic mutations will fail to be identified before diagnosis and treatment.[11,19,24] In addition, some patients who do meet criteria for genetic testing decline testing or fail to pursue it.[2,28] Insurance companies may also refuse coverage for genetic testing for breast cancer.[29] Therefore, not all patients who qualify for genetic testing undergo it, and those who do not meet testing criteria may harbor a pathogenic mutation.[7,27,30]

From a reconstructive standpoint, an unidentified pathogenic mutation at the time of unilateral mastectomy is especially problematic for patients opting for abdominally based free flap breast reconstruction, as this donor site can be used only once. If a deleterious mutation is discovered later and contralateral prophylactic mastectomy is recommended, the patient must undergo additional procedures and the abdomen is no longer an option as a donor site. Alternatives, such as implant-based reconstruction or nonabdominal donor sites, may be available but problematic for various reasons.[31–35] The purpose of this study was to determine (1) the frequency of genetic testing before unilateral abdominally based free flap breast reconstruction, (2) the frequency of mutations detected in patients undergoing unilateral abdominally based free flap breast reconstruction, and (3) the cost-effectiveness of expanding genetic testing in this patient population.

PATIENTS AND METHODS

Patient Selection

After obtaining approval from the Institutional Review Board of Brigham and Women's Hospital/Dana-Farber Cancer Institute, we performed a retrospective review to identify all breast cancer patients who underwent unilateral abdominally based free flap breast reconstruction at Brigham and Women's Hospital/Dana-Farber Cancer Institute between September of 2007 and April of 2016. Patients who underwent either deep inferior epigastric perforator (DIEP), muscle-sparing free transverse rectus abdominis musculocutaneous, free transverse rectus abdominis musculocutaneous, or superficial inferior epigastric artery perforator flap surgery were included. Those who underwent free flap breast reconstruction from a nonabdominal donor site were excluded. Also excluded were patients who underwent unilateral reconstruction for prophylactic indications, such as a pathogenic mutation in a patient who had already had a contralateral mastectomy.

Data Collection

Clinical data were obtained from the electronic medical record, and an assessment was made on whether each patient met 2016 National Comprehensive Cancer Network guideline criteria for genetic testing. An independent Dana-Farber Cancer Institute database of genetic test results was queried for completeness. Length of follow-up was calculated by looking at the time between free flap breast reconstruction and the last clinical encounter documented. To ensure accuracy, all extracted data was checked by a second reviewer. Descriptive statistics were then calculated. Financial information was obtained from the Brigham and Women's Hospital Billing Department and from the Dana-Farber Cancer Institute Center for Cancer Genetics and Prevention.

RESULTS

Clinical Characteristics

Between 2007 and 2016, 713 patients underwent free flap breast reconstruction, and of these,

Table 1. Clinical Characteristics of the Patient Cohort

Variable	No. (%)
No. of patients	160
Age at first diagnosis	
≤45 yr	57 (35.6)
46–50 yr	46 (28.8)
51–60 yr	46 (28.8)
≥61 yr	11 (6.8)
Premastectomy stage	
DCIS/0	49 (30.6)
1	51 (31.9)
2	33 (20.6)
3	9 (5.6)
4	0
Unknown or other	18 (11.3)
Postmastectomy stage	
0	36 (22.5)
1	57 (35.6)
2	34 (21.2)
3	12 (7.5)
4	0
Unknown/other*	21 (13.1)
Receptor status	
ER-positive	115 (71.9)
PR-positive	101 (63.1)
Her-2/Neu-positive	32 (20)
Triple-negative	9 (5.6)
Chemotherapy	
None	39 (24.4)
Premastectomy	29 (18.1)
Postmastectomy	69 (43.1)
Premastectomy and postmastectomy	23 (14.4)
Radiation therapy	
None	90 (56.3)
Premastectomy	52 (32.5)
Postmastectomy	18 (11.3)
Timing of reconstruction	
Immediate	113 (70.6)
Delayed-immediate	19 (11.9)
Delayed	25 (15.6)
Unplanned conversion to FFBR	3 (1.9)

ER, estrogen receptor; PR, progesterone receptor; Her2/Neu, human epidermal growth factor receptor 2; DCIS, ductal carcinoma in situ; FFBR, free flap breast reconstruction.
*The most common reason for unknown stage was the patient presented for delayed reconstruction having undergone mastectomy at a different hospital.

160 met inclusion criteria. Table 1 lists the clinical characteristics of our patient cohort. The timing of reconstruction was immediate in 113 patients (70.6 percent), delayed-immediate in 19 patients (11.9 percent), and delayed in 25 patients (15.6 percent), with average follow-up time of 69 months (range, 23 to 119 months).

Testing Criteria and Status

We examined whether patients met 2016 National Comprehensive Cancer Network guidelines for genetic testing at the time of free flap breast reconstruction and whether testing occurred before free flap breast reconstruction. We found that 62 of 111 patients (55.9 percent) who met 2016 National Comprehensive Cancer Network guidelines at the time of free flap breast reconstruction were tested, whereas 49 of 111 patients (44.1 percent) who met criteria were not tested. Of the 49 patients who did *not* meet National Comprehensive Cancer Network guidelines for testing before free flap breast reconstruction, 44 of 49 (89.8 percent) were not tested before free flap breast reconstruction and five of 49 (10.2 percent) were tested. Figure 1 depicts this distribution of patients.

Genetic Mutations Identified in Patient Cohort

We identified eight genetic mutations in six patients, and these are summarized in Table 2. The three deleterious mutations detected after free flap breast reconstruction (two *BRCA2* and one *ATM1)* resulted in contralateral mastectomy and reconstruction. Another three patients were found to have five variants of uncertain significance and one deleterious mutation, and in these cases, mastectomy was not pursued and they received close surveillance. The clinical course of the six patients is described in cases 1 through 6.

CASE REPORTS

Case 1

The patient in case 1 was diagnosed with a second breast primary tumor at age 53 after undergoing breast-conserving therapy at age 46. She had a significant smoking history and a family history of breast, ovarian, and pancreatic cancer. She was referred for genetic testing; however, her insurance company denied coverage and the patient could not afford the costs out-of-pocket. She underwent a unilateral mastectomy and immediate DIEP flap reconstruction, followed by revision, nipple reconstruction, and a contralateral augmentation. Her daughter was found to have a deleterious *BRCA2* mutation, and this led to the discovery of the same *BRCA2* mutation in the patient. She opted for close surveillance but was found to have contralateral ductal carcinoma in situ 1 year later. She underwent contralateral mastectomy and tissue expander placement but postoperatively developed mastectomy flap necrosis requiring excision, and cellulitis, and ultimately her tissue expander was removed. She has been unable to proceed with additional reconstruction because of financial constraints and limited sick time.

Case 2

The patient in case 2 was diagnosed with microinvasive ductal carcinoma in situ at age 60. She had no family history of cancer and did not meet National Comprehensive Cancer Network criteria for genetic testing. She underwent unilateral mastectomy and immediate DIEP flap reconstruction, followed by revision and nipple reconstruction. Her daughter was found to have a *BRCA2* mutation, which led to the identification of a deleterious *BRCA2* mutation in the patient. Three years after her initial DIEP flap, she underwent a right mastectomy and tissue expander placement. A few months later, her expander was exchanged and her DIEP flap revised for symmetry.

Case 3

The patient in case 3 was diagnosed with ductal carcinoma in situ at age 44. She had a strong family history of breast cancer

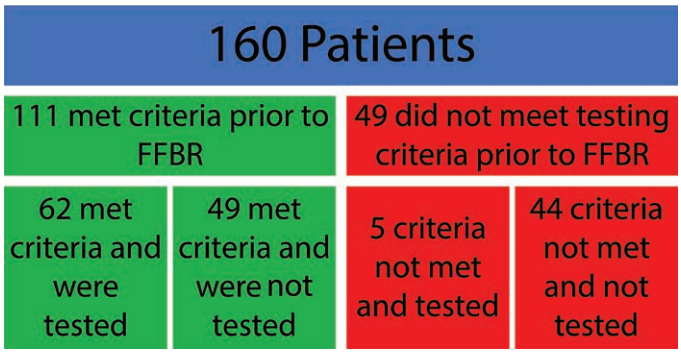

Fig. 1. Breakdown of patients according to whether 2016 National Comprehensive Cancer Network criteria for genetic testing were met and whether testing occurred before unilateral abdominally based free flap breast reconstruction (*FFBR*).

Table 2. Genetic Mutations Discovered in Patients Undergoing Unilateral Abdominally Based Free Flap Breast Reconstruction*

Genetic Mutation	No. of Mutations	Timing of Detection of Mutation	Contralateral Mastectomy Recommended
Pathogenic mutations			
BRCA1	0	N/A	N/A
BRCA2	2	After free flap × 2	Yes
ATM	2	One before, one after	Variable
Variants of uncertain significance			
BRCA1	0	N/A	N/A
BRCA2	2	Before free flap × 2	No
ATM	1	Before free flap	No
CDH1	1	Before free flap	No
CHEK-2	1	Before free flap	No
STK11	1	Before free flap	No

N/A, not applicable.
*Eight mutations were discovered in six patients.

and *BRCA1/2* testing was negative. She underwent unilateral mastectomy and immediate DIEP flap reconstruction, followed by multiple revisions for symmetry. Three years later, more extensive genetic testing identified a pathogenic mutation in her *ATM* gene. Based on her strong family history, she opted for a contralateral prophylactic mastectomy. She underwent mastectomy and immediate stacked profunda artery perforator flaps. Her postoperative course was complicated by venous congestion requiring two operative reexplorations with salvage of both flaps.

Case 4

The patient in case 4 was diagnosed with multifocal breast cancer at age 35. She had a strong family history of breast cancer and underwent genetic testing for *BRCA1/2* before free flap breast reconstruction. She was found to have a variant of uncertain significance in *BRCA2* and contralateral prophylactic mastectomy was not recommended. The patient proceeded to unilateral mastectomy and reconstruction.

Case 5

The patient in case 5 was diagnosed with breast cancer at age 47. Because of a family history of breast and pancreatic cancer, she was referred for genetic testing, which revealed a deleterious mutation in *ATM* and a variant of uncertain significance in *ATM* and *CHEK2*. The patient opted for close surveillance rather than contralateral prophylactic mastectomy and underwent unilateral mastectomy and reconstruction.

Case 6

The patient in case 6 was diagnosed with breast cancer at age 31, and her family history was notable for breast cancer. Genetic testing performed before free flap breast reconstruction revealed a variant of uncertain significance in *BRCA2* and *STK11*, and the patient proceeded to unilateral mastectomy and reconstruction.

Summary

In summary, of the three patients who were diagnosed with deleterious genetic mutations after free flap breast reconstruction who proceeded to contralateral mastectomy and reconstruction, one met National Comprehensive Cancer Network guidelines and was not tested, one did not meet National Comprehensive Cancer Network guidelines and was not tested, and one was tested for

Table 3. Number of Patients Who Met 2016 National Comprehensive Cancer Network Criteria for Genetic Testing Stratified by Year of Unilateral Abdominally Based Free Flap Breast Reconstruction, and According to Whether Testing Occurred before or after That Procedure

Year of Reconstruction	Patients Who Met NCCN Criteria for Testing	Tested before Unilateral FFBR (%)	Tested after Unilateral FFBR (%)	Not Tested to Date (%)
2007	4	1 (25)	2 (50)	1 (25)
2008	10	4 (40)	3 (30)	3 (30)
2009	14	7 (50)	7 (50)	0
2010	7	2 (28.6)	1 (14.3)	4 (57.1)
2011	13	7 (53.8)	1 (7.7)	5 (38.5)
2012	15	7 (46.7)	3 (20)	5 (33.3)
2013	16	9 (56.2)	1 (6.3)	6 (37.5)
2014	12	11 (91.7)	1 (8.3)	0
2015	8	6 (75)	0	2 (25)
2016	12	7 (58.3)	0	5 (41.7)
All	111	61 (55)	19 (17)	31 (28)

BRCA1/2 only with a later extended panel revealing a mutation. Of note, all three patients had adequate infraumbilical adiposity for bilateral free flap breast reconstruction.

Frequency of Genetic Testing by Year

We examined the rates at which patients who met National Comprehensive Cancer Network criteria were tested by calendar year in which reconstructive surgery was performed. These results are presented in Table 3. On average, 55 percent of patients met National Comprehensive Cancer Network guidelines for testing before free flap breast reconstruction. There was a trend toward an increased percentage of patients who met National Comprehensive Cancer Network guidelines undergoing testing before abdominally based free flap breast reconstruction in earlier years, with 39.5 percent undergoing testing between 2007 and 2011, and 65.6 percent undergoing testing between 2012 and 2016.

COST ANALYSIS

Additional Costs Arising from the Delayed Detection of Deleterious Mutations

The billing records for the three patients with pathogenic mutations discovered after free flap breast reconstruction were reviewed to identify additional costs generated by the delayed identification of genetic mutations; these results are presented in Table 3. These dollar figures reflect actual payments to the hospital and not charges.

Costs Related to Expanding Genetic Testing before Abdominally Based Free Flap Breast Reconstruction

To estimate the increased costs from more extensive genetic testing before unilateral abdominally based free flap breast reconstruction, we identified a price point for individual genetic testing. In the current marketplace, there is a minimal cost differential between testing for *BRCA1/2* alone and multigene panel testing. Thus, we used the cost of extended panel testing, which is $1000 for insured patients at our institution [using Invitae (San Francisco, Calif.), which charges contracted insurance companies $1000]. Uninsured patients can obtain a direct-to-consumer saliva-based test (Color Genomics Hereditary Cancer Test) for $250, which detects mutations in 12 genes known to predispose to breast cancer.[36] For our cost analysis, we used the higher price for genetic testing of $1000 to model the maximal cost that would be encountered. Of the cohort of 160, 67 patients were tested and 93 patients were not tested before free flap breast reconstruction. Therefore, expanding testing to all patients before free flap breast reconstruction would have resulted in an increased cost of 93 patients times $1000/patient = $93,000.

Estimated Net Costs of Expanding Genetic Testing before Unilateral Abdominally Based Free Flap Breast Reconstruction

If all patients were offered genetic testing and those with deleterious mutations underwent bilateral mastectomy with abdominally based free flap breast reconstruction, the additional costs would be $93,000 (for genetic testing) and potentially $355,760 would be saved (see additional costs outlined in Table 4). This would result in a net savings of $262,760 ($355,760 minus $93,000).

DISCUSSION

The present study identified 1.9 percent of patients (three of 160) who were diagnosed with

Table 4. Additional Costs Resulting from the Identification of Deleterious Genetic Mutations for Breast Cancer Detected after Abdominally Based Free Flap Breast Reconstruction, Based on Hospital Billing Data*

Types of Additional Costs	Total Amount
Case 1	$108,265
Office visits after mutation identified	
Professional fees for contralateral mastectomy/immediate tissue expander placement (i.e., breast surgeon, plastic surgeon, anesthesiologist, pathologist), excision of mastectomy flap necrosis (i.e., plastic surgeon), and eventually removal of tissue expander (i.e., plastic surgeon, anesthesiologist)	
Hospital fees for operating room and admission for contralateral mastectomy/expander, admission for left breast cellulitis, and later for operating room and admission for removal of tissue expander	
Case 2	$43,900
Office visits after mutation identified	
Professional fees for contralateral mastectomy/immediate tissue expander placement (breast surgeon, plastic surgeon, anesthesiologist, pathologist), and exchange of tissue expander for permanent implant (plastic surgeon, anesthesiologist)	
Hospital fees for operating room and admission for contralateral mastectomy and operating room for exchange of tissue expander for permanent implant	
Case 3	$203,595
Office visits after mutation identified	
CTA with radiology read to evaluate perforators	
Professional fees for contralateral mastectomy and stacked PAP flaps (breast surgeon, plastic surgeon, anesthesiologist, pathologist), and two operative explorations of reconstructed breast (plastic surgeon and anesthesiologist), and revision of reconstructed breast (plastic surgeon and anesthesiologist)	
Hospital fees for operating room (three times) and admission for contralateral mastectomy and stacked PAP flaps, and for operating room for revision procedure	
Total additional cost for all three cases	$355,760

CTA, computed tomographic angiography; PAP, profunda artery perforator.
*Dollar figures are actual payments received by the hospital and not charges.

deleterious genetic mutations after unilateral abdominally based free flap breast reconstruction who proceeded to have contralateral mastectomy and reconstruction during a relatively short follow-up period. Post–free flap breast reconstruction genetic testing was prompted by discovery of deleterious mutations in an offspring in some cases, resulting in additional operations after completed multistage reconstructions and psychosocial and financial burdens for patients and costliness for the health care system. Based on a recent study at our institution where genetic testing was performed for all stage I to III patients, we expect the rate of pathogenic mutations to be close to 10.7 percent.[1] Therefore, although the post–free flap breast reconstruction discovery of pathogenic mutation is a low-frequency event, its rate will likely rise with time and has a large impact because of the high cost of additional surgery.

Our results showed that only 55.9 percent of patients of patients who met 2016 National Comprehensive Cancer Network guidelines for genetic testing had documented results of testing. Potential explanations for this seemingly low incidence of testing include that results from outside institutions may have been omitted from the medical record, that patients declined testing, or that insurance companies could have denied coverage. Also possible is that oversight by clinicians occurred, such as failing to calculate initial age at diagnosis for a patient with a history of breast cancer and a new primary tumor, or the age of initial diagnosis for a patient who presents for delayed reconstruction, or failing to recognize two primary tumors as qualifying for testing.[14,23]

Because the National Comprehensive Cancer Network guidelines are complicated and difficult to remember, offering testing to all candidates for unilateral abdominally based free flap breast reconstruction is simpler and, our data show, also cost-effective. There are multiple potential and expected risks and benefits to expanding genetic testing before abdominally based free flap breast reconstruction, and these are summarized in Table 5. If insurance companies deny coverage for genetic testing, our results could be used to support coverage of these tests. In addition, patients who qualify for genetic testing but who decline it should be counseled that they run a small risk of needing a contralateral prophylactic mastectomy and reconstruction after completing free flap breast reconstruction, with associated financial and other burdens.[16,24,37]

Prior studies have looked at the cost-effectiveness of expanding genetic testing for breast cancer. One group demonstrated that for every 10,000 women screened for *BRCA* mutations, approximately four cases of breast cancer and two cases of ovarian cancer could be averted over what family history-based testing would elucidate.[30,38–40]

Table 5. Potential Effects of Offering Genetic Testing to All Patients Who Present for Unilateral Abdominally Based Free Flap Breast Reconstruction*

	Costs	Savings
Financial impact to the health care system	Expected: • Increased cost of genetic testing, $1000/insured patient and $250/uninsured patient • Professional fees for contralateral mastectomy and FFBR (however, contralateral surgery is usually billed at 50% when performed the same day) • Hospital fees for additional time spent in the operating room for bilateral abdominally based FFBR Potential: • Cost of treating complications on the contralateral side, microsurgical or otherwise	Expected: • Eliminate second hospitalizations for contralateral mastectomy and reconstruction • Avoid need for implant-based reconstruction and associated complications in suboptimal implant candidates • Avoid need for stacked free flaps and free flaps with known higher complication rates (i.e., GAP flap) Potential: • Fewer number of revisions, as patients will be more symmetric after initial surgery
Other risks and benefits	Risks Expected: • Waiting for genetic results can delay mastectomy/FFBR • Patient anxiety while waiting for test results • Psychological burden if deleterious mutation discovered Potential: • Known genetic mutation theoretically could negatively affect future health insurance policies	Benefits Expected: • Decreased risk of contralateral breast cancer • Improved symmetry of reconstructed breasts • Family members alerted to the potential need to undergo genetic testing Potential: • More cost-effective for patient as deductibles met once and avoid second large deductible • Less likely to exhaust sick leave because of need for second hospitalization and recovery

FFBR, free flap breast reconstruction; GAP, gluteal artery perforator.
*Patients who opt for preoperative genetic testing and are found to have deleterious mutations would proceed to bilateral mastectomy and immediate abdominally based free flap breast reconstruction.

Long and Ganz suggested that with a cost of $4000 per test, the cost of *BRCA* testing would need to drop by 90 percent to make universal testing cost-effective for the general population.[41] Kwon et al. project the highest life expectancy when testing all women with breast cancer younger than 50 years.[10,11] However, the authors suggest that the cost associated with this approach may be prohibitive, with an incremental cost-effectiveness ratio of $59,503 and $112,908 per year of life and quality-adjusted life-year gained, respectively.[10,11] This group supports adopting the next most practical strategy, which is to test women younger than 50 with triple-negative breast cancers, which had a favorable cost-effectiveness—below the acceptable threshold of $50,000 per year of life gained.[10,11] However, several factors make our cohort and cost-to-benefit ratio different from these prior studies. First, the cost of genetic testing has declined since these articles were written, as private companies now offer a panel of tests for as little as $250.[30,40,41] Second, none of these studies focused on a subset of patients undergoing a complex and expensive type of reconstruction such as abdominally based free flap breast reconstruction, which can balance out the now vastly reduced cost of extended panel genetic testing.[10,11,30,38–41]

Further commentary is warranted on the finding that two patients with deleterious *ATM* mutations differed with regard to contralateral surgery. One mutation was detected after free flap breast reconstruction and the patient had contralateral prophylactic mastectomy and reconstruction. The other patient's mutation was found before free flap breast reconstruction, and contralateral prophylactic mastectomy was not performed. *ATM* is an example of a recently discovered gene whose breast cancer risk is not clearly established, and so decisions about contralateral prophylactic mastectomy are individualized based on family history and other factors.[42] According to the 2016 National Comprehensive Cancer Network guidelines, there is sufficient evidence to support more frequent screening with *ATM* but insufficient evidence to support contralateral prophylactic mastectomy. However, contralateral prophylactic mastectomy should be considered in the context of the patient's family history. Recommendations will continue to evolve over time as more long-term data are accrued.

Weaknesses and Limitations

There are several weaknesses of the present study. First, it is possible that we underestimated the percentage of patients who underwent testing before abdominally based free flap breast reconstruction because patients failed to report or were not aware of genetic testing performed at outside institutions.

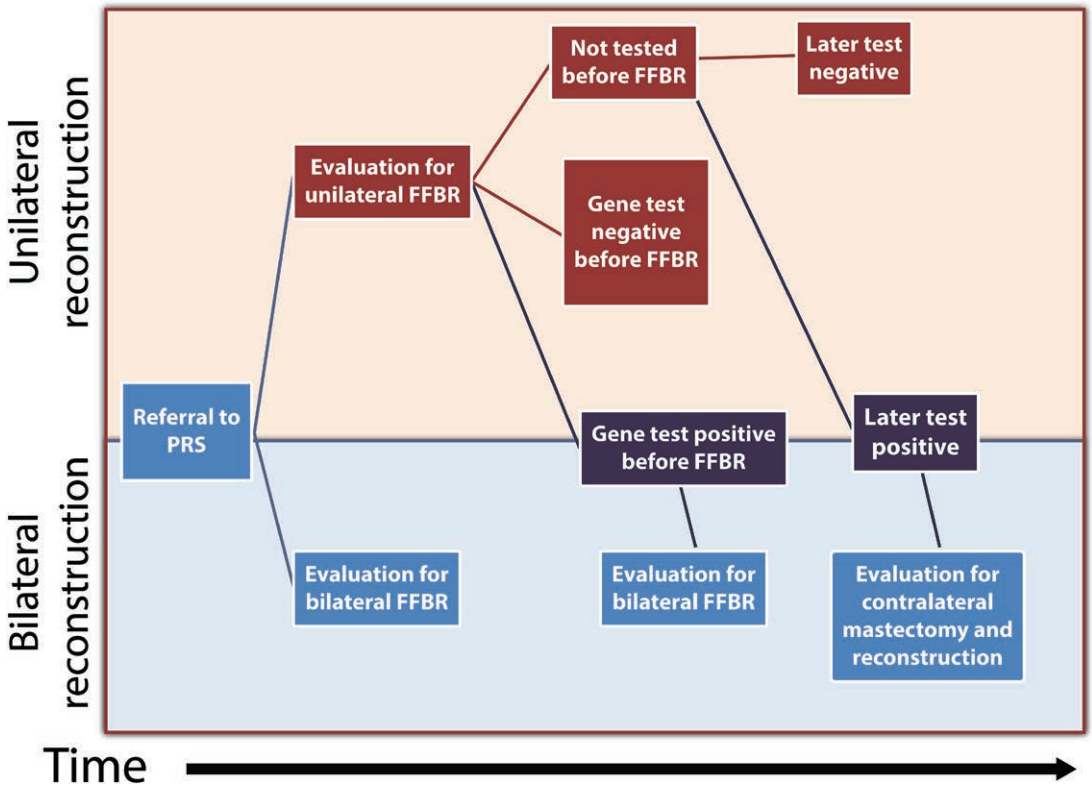

Fig. 2. The impact of the timing of genetic testing for breast cancer and abdominally based free flap breast reconstruction (*FFBR*). Patients with pathogenic mutations who test positive before free flap breast reconstruction are referred for bilateral mastectomies and reconstruction. This patient population was not captured by the current study because of retrospective identification of unilateral abdominally based free flap breast reconstruction cases.

Second, its retrospective nature means we did not capture patients who presented for unilateral reconstruction, but who were found to have pathogenic mutations and subsequently underwent bilateral abdominally based free flap breast reconstruction (Fig. 2). A prospective study would be needed to determine the rate at which conversion from unilateral to bilateral reconstruction occurs based on genetic testing. Third, not every patient had genetic testing, so the true incidence of pathogenic mutations in this patient population is unknown. Only prospective testing of consecutive patients would determine the actual incidence of mutations. Fourth, this study did not address whether it is clinically appropriate and cost-effective to offer extended panel testing preoperatively to patients who have already undergone testing for *BRCA1/2*.

CONCLUSIONS

Traditionally, the need for referral for genetic testing for breast cancer patients has been determined by oncologic features and family history, and not by reconstructive procedure planned. However, this study supports the notion that genetic testing should be offered to all patients for whom a unilateral abdominally based free flap breast reconstruction is planned. Plastic surgeons should take an active role in discussing with patients and their care providers the implications of genetic testing in these cases. As greater numbers of deleterious genetic mutations are discovered, more patients may be affected by positive results. Close communication with genetic counselors is crucial as the complexity in this area continues to grow.

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