Knowledge and Attitudes about Microsatellite Instability Testing among High-Risk Individuals Diagnosed with Colorectal Cancer

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Abstract

For individuals meeting Bethesda criteria for hereditary nonpolyposis colorectal cancer syndrome, the microsatellite instability (MSI) test is recommended as a screening evaluation before proceeding to genetic testing. The MSI test is new to the medical setting, but will be increasingly used to screen patients at high risk for hereditary nonpolyposis colorectal cancer. The main goals of this study were to examine knowledge about and exposure to the MSI test among individuals considering the test, to evaluate perceived benefits and barriers to undergoing the MSI test, and to identify the demographic, medical, and psychosocial correlates of the perceived benefits and barriers to undergoing the test. One hundred and twenty-five patients completed a survey after being offered the test, but prior to making the decision whether to pursue MSI testing. Results indicated low levels of knowledge about and previous exposure to the MSI test. Participants held positive attitudes about the potential benefits of the test and perceived few barriers to undergoing the test. Motivations were similar to those cited by individuals considering other genetic tests. Participants with nonmetastatic disease, with lower perceived risk for cancer recurrence, and who reported more self-efficacy endorsed more benefits from the test. Higher levels of cancer-specific psychological distress were associated with more perceived barriers to having the test. These findings suggest that individuals considering the MSI test know very little about it but hold positive attitudes about the test's utility. More distressed patients, patients who perceive themselves at higher risk for cancer recurrence, and patients with metastatic disease might be less motivated to have the MSI test. (Cancer Epidemiol Biomarkers Prev 2007;16(10):2110–7)

Introduction

Hereditary nonpolyposis colorectal cancer (HNPCC), also called Lynch syndrome, is an autosomal dominant disorder and is the most common hereditary cause of colorectal cancer. Although HNPCC accounts for only ~5% of colorectal cancers, the identification of this syndrome is particularly important as there are significant implications not only for their genetic testing, screening, and management of probands, but also for their family members.

HNPCC is caused by germ line mutations in one of several mismatch repair genes including *MLH1, MSH2, MSH6*, and *PMS2*. The function of these genes is to maintain the integrity of the genome by ensuring the fidelity of DNA replication through effective mismatch repair. A mutation in any one of the mismatch repair genes causes genomic instability and susceptibility to colon and other HNPCC-related cancers. Defective mismatch repair can lead to changes in the length of DNA repeat sequences in tumor compared with normal tissue, known as microsatellite instability (MSI). The MSI test is recommended as a screening evaluation before proceeding to genetic testing for individuals meeting clinical criteria for HNPCC (1, 2). Commonly used clinical criteria for HNPCC are the so-called ''Amsterdam criteria'' and ''Bethesda criteria.'' In order to qualify, the Amsterdam criteria requires that families have three or more persons affected with an HNPCC-related cancer (one is a first-degree relative of the other two), that the cancers in the family span two generations, and that at least one case is <50 years old (2, 3). These stringent criteria have high specificity but low sensitivity for the detection of HNPCC. Therefore, the less rigid Bethesda criteria was established to help select patients whose tumor could be first screened for MSI (and/or immunohistochemistry to detect loss of expression of mismatch repair proteins) prior to pursuing germ line genetic testing (Bethesda Criteria are described further in Materials and Methods; ref. 4).

MSI is a phenotype present in the tumor of patients with HNPCC. MSI is graded as high, low, or stable. In the appropriate clinical setting, patients with MSI-high tumors are subsequently referred for genetic testing. Although the MSI test is highly sensitive for HNPCC, it lacks specificity as MSI-high histologies occur in ~15%

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of sporadic colorectal tumors. Thus, formal genetic testing is required to confirm this diagnosis. Based on a variety of guideline recommendations (e.g., refs. 5, 6), it is likely that MSI testing will be increasingly used as a screening test to determine whether individuals are likely to have HNPCC. However, because the MSI test lacks specificity, results may have a fair degree of uncertainty associated with them. Assisting patients in understanding the complex nature of this information is an important goal.

Because the MSI test is new to the medical setting, very little is known about the level of knowledge among individuals considering the test. It is the only ''screening'' test, in addition to immunohistochemistry, that is currently offered in the cancer genetics setting. Therefore, it is important to explore patient motivations about the utility of this information and reasons to pursue further genetic testing. There have been no studies characterizing individuals' motivations for wanting to undergo or not undergo MSI testing. Because the MSI test will increasingly be used in clinical settings, it is important that individuals understand the purpose and limitations of the test in order to make a well-informed decision about whether to pursue testing. One component of an informed decision is an understanding of personal motivations to have or not have the test. Prior research on genetic tests for HNPCC among at-risk individuals have suggested several potential motivations, including clarification of the risk for children and other relatives (7, 8), and guidance on decisions regarding preventive health behaviors (7, 9, 10). Negative consequences are typically considered as well, because test results can cause emotional distress and affect life choices such as childbearing decisions (11). For those who pursue HNPCC testing and ultimately test positive for mutations, insurance and employment discrimination concerns may also be present (12). Other barriers to having genetic testing have included the inaccuracy of results (7, 10). This issue is particularly relevant to the MSI test, as even ''positive'' test results are associated with uncertainty about whether a germ line mutation is likely to be present.

We undertook a randomized clinical trial to examine the efficacy of an educational CD-ROM versus basic information in increasing the level of knowledge and preparedness of individuals considering MSI testing. The present report summarizes information regarding knowledge and motivations for and against having this test at the baseline time point (pre-education), and characterizes attitudinal and nonattitudinal factors associated with individuals' motivations to have or not have the MSI test.

We examined five attitudinal factors associated with motivations: perceived cancer risk, self-efficacy, psychological distress, and perceived physician support and perceived family support for MSI testing. Our selection of attitudinal variables was guided by the Health Belief Model (13, 14), the Dual Process Theory (15, 16), and the Theory of Planned Behavior (17). From the Health Belief Model, we adopted the construct of perceived risk. Previous research evaluating the association between risk and perceived benefits and barriers has been inconsistent. Some studies indicate that greater perceived cancer risk is associated with greater perceived barriers to genetic testing and skepticism about the utility of genetic tests (18, 19). However, studies examining other health behaviors indicate that greater perceived risk is associated with greater perceived benefits of risk-reducing behaviors (20). We adopted two constructs from the Dual Process Theory (15), psychological distress responses to the diagnosis of cancer and self-efficacy. Although previous research has not explicitly evaluated the association between cancer-related distress and perceived benefits and barriers to genetic screening or testing, previous research among unaffected women has suggested that worry about cancer risk is associated with the formation of positive attitudes about the protective benefits of testing (19). Self-efficacy is the individual's confidence in his or her ability to successfully engage in a specific behavior (21). Although not studied as a correlate of perceived benefits and barriers of genetic testing, less perceived confidence/self-efficacy to perform protective health behaviors is a known correlate of greater barriers to engagement in health behaviors such as sun protection (e.g., ref. 20).

We also considered social influence, a key factor in the Theory of Planned Behavior. Two main social influence variables are physician and family member support for undergoing testing. Although not studied in the context of genetic testing, physician and family support for cancer screening practices have been significantly associated with fewer perceived barriers and greater perceived benefits of engaging in screening (e.g., ref. 22). Finally, knowledge about the MSI test is likely to influence perceived benefits. Individuals who know more about the purpose and possible results of the test are likely to endorse greater benefits. Indeed, previous research has suggested that knowledge about genetic tests is associated with greater perceived benefits of testing (23).

We based our predictions regarding the associations between study constructs on Hershey[4] and Ronis and colleagues' (24, 25) elaborations of the Health Belief Model. They proposed that perceived benefits are directly influenced by perceived risk and perceived severity. Neither risk nor severity was hypothesized to relate with perceived barriers. Support for this elaborated model has been inconsistent, with some cancer screening studies suggesting that risk and severity are associated with benefits but not barriers (20, 26, 27), and some cancer screening studies suggesting that severity is associated with barriers but not benefits (22). Later elaborations to this model have included other factors likely to influence perceived benefits and barriers, including physician and family support for colorectal cancer screening and psychological distress (22), and found that family and physician support predicts both benefits and barriers. Based on these findings, as well as Ronis and colleagues' elaborated model, we examined potential correlates of perceived benefits and barriers separately, and included additional constructs such as physician and family support for testing, knowledge, previous media exposure to the MSI test, psychological distress, and self-efficacy, which are potentially important correlates of motivations to have the MSI test.

[4] J. Hershey. Formalization of the Health Belief Model: measuring health beliefs in compliance studies. Philadelphia: University of Pennsylvania; 1979. Unpublished working paper.

The present study had three aims. The main aim was to characterize the level of knowledge about the purpose and results of the MSI test among individuals considering this test, and to describe the level of previous exposure to information about the MSI test. We predicted that the level of knowledge and exposure to information about the MSI test would be extremely low. The second aim of the study was to characterize motivations for (perceived benefits) and against (perceived barriers) having the MSI test. We predicted that patients would hold a high level of positive beliefs about the benefits and utility of the test and relatively low levels of negative beliefs about the disadvantages of the MSI test. The third aim was to examine the contribution of attitudinal and nonattitudinal variables to perceived benefits and barriers of MSI testing. We focused on five attitudinal correlates: perceived risk for cancer recurrence, self-efficacy, cancer-specific distress, perceived physician support for MSI testing, and perceived family support for MSI testing with perceived benefits and barriers of MSI testing. In terms of nonattitudinal correlates, the role of demographic, medical risk factors (e.g., number of relatives with cancer), and MSI knowledge and media exposure were evaluated. As noted previously, the correlates of perceived benefits and barriers were examined separately.

Materials and Methods

Participants. One hundred and twenty-five individuals were chosen to participate and were offered MSI testing. These individuals met the Revised Bethesda criteria (4), which included (*a*) colorectal cancer diagnosed in a patient who is <50 years of age; (*b*) presence of synchronous or metachronous colorectal, or other HNPCC-associated tumors, regardless of age; (*c*) colorectal cancer with MSI-high histology diagnosed in a patient who is <60 years of age; (*d*) the proband has two or more first- or second-degree relatives with an HNPCC-related tumor, with one of the cancers being diagnosed under the age of 50 years; or (*e*) colorectal cancer diagnosed in two or more first- or second-degree relatives with HNPCC-related tumors regardless of age. Participants were excluded if they met more stringent Amsterdam criteria for Lynch syndrome.

The characteristics of the participants are shown in Table 1. The majority of participants were married, Caucasian, middle income, and relatively well educated. The majority of the samples were diagnosed within the past 2 years (71%) and almost half of the samples were diagnosed with stage IV disease.

Procedures. Participants were enrolled at two National Cancer Institute–designated comprehensive cancer centers and one community hospital cancer center. Potentially eligible participants were identified from medical records, and the attending physician was asked to discuss the study with the patient if MSI testing was clinically indicated. Physicians informed the patient that they might have HNPCC and described the MSI test as a screening test. Next, the physician described the study as a method of helping them understand the purpose and meaning of the MSI test. If the patient was interested, s/he was referred to the study research assistant, who described the study in detail. Written informed consent was signed and the participant completed the baseline survey that formed the basis of this report. Participants completed the survey in person in the hospital clinic with assistance from the research assistant if requested. This analysis is the initial portion of a randomized clinical trial to evaluate the efficacy of an educational CD-ROM on MSI testing on knowledge and attitudes about the test.

Table 1. Characteristics of participants (*n* = 125)

Characteristic	*N* (%)
Gender	
Male	71 (56.8)
Female	54 (43.2)
Age (y)	
Mean (SD)	44.65 (6.14)
Race/ethnicity	
White	110 (88.0)
Black/African American	8 (6.4)
Asian/Pacific Islander	2 (1.6)
Hispanic	2 (1.6)
Other	3 (2.4)
Education	
High school graduate or less	24 (19.2)
Some college/trade school/business school	56 (44.8)
4-y degree	14 (11.2)
Some graduate education	3 (2.4)
Graduate degree	28 (22.4)
Annual household income (in U.S. dollars)	
Mean	$60,0000-99,999
Site of primary cancer	
Colon	85 (60.0)
Rectum	37 (29.6)
Rectosigmoid	13 (10.4)
Years since cancer diagnosis	
Mean (SD)	1.64 (2.28)
Cancer stage	
Stage I	11 (8.8)
Stage II	22 (17.6)
Stage III	43 (34.4)
Stage IV	43 (34.4)
Uncertain	6 (4.8)
Metastatic disease	60 (48.0)
ECOG performance status	
0	100 (80)
1	25 (20)

One hundred and seventy-three individuals were approached for participation. Of these, 125 individuals consented and completed the baseline survey (72%), 36 individuals refused the study (20.8%), and 13 individuals signed a consent form but did not complete a baseline survey (7.5%). The majority of patients did not provide a reason for refusal. Among those providing a reason, the most common reason was ''too busy'' (9%). Comparisons between study participants and refusers indicated that refusers had poorer Eastern Cooperative Oncology Group (ECOG) status ratings (0 = fully active, 1 = restricted in strenuous activity, ambulatory; 2 = ambulatory but unable to work; 3 = capable of limited self-care, confined to bed or chair >50% of waking hours; 4 = completely disabled) compared with study participants [χ^2 (1) = 21.4, N = 173, $P < 0.001$, ECOG $\geq 1_{\text{refusers}}$ = 60.6%, ECOG $\geq 1_{\text{participants}}$ = 19.5%]. There were no differences with regard to age, time since diagnosis, or ethnicity.

Outcome Measures

MSI Knowledge. This 17-item face-valid true-false measure was developed for the present study. Items assessed knowledge about the purpose and nature of

MSI testing as well as basic knowledge about colon cancer genetics (e.g., ''When cells in my body cannot repair mistakes that occur in DNA, it causes microsatellite instability''). The score was calculated as the percentage of correct answers (0-100%). Internal consistency, as calculated by Cronbach's α, was 0.90.

Exposure to Information about MSI Testing. Four face-valid items developed for the present study assessed whether or not the participant read articles about MSI testing in magazines or newspapers, television, the Internet, or radio (yes/no). Because there were so few participants who had more than one item endorsed, the item was dichotomized for purposes of this analysis (any item endorsed or no item endorsed).

Perceived Benefits of MSI Testing. A 14-item measure was adapted from a *BRCA1* and *BRCA2* benefits and barriers measure (28). Additional items were added to address the specific benefits of MSI testing. Items were rated on a four-point Likert scale (1 = strongly disagree, 4 = strongly agree). A sample benefits item is, ''Because I want to learn if my children and other biological relatives are at risk for developing colorectal cancer.'' Internal consistency, as calculated by Cronbach's α, was 0.86.

Perceived Barriers of MSI Testing. A 10-item measure was adapted from a *BRCA1* and *BRCA2* barriers measure (28). Additional items were added to address specific barriers of MSI testing. Items were rated on a four-point Likert scale. A sample barrier was, ''Because I do not want to know what my family members' risk for colorectal cancer might be.'' Internal consistency, as calculated by Cronbach's α, was 0.84.

Psychosocial Correlates: Risk, Efficacy, Distress, Family, and Physician Support for Testing

Perceived Colorectal Cancer Risk. Two items developed by Lerman et al. (29, 30) assessed risk: how the diagnosis affected perceived risk of developing a recurrence of colorectal cancer and the chances of getting any type of cancer again in the participant's lifetime. Both items were rated by asking the participant to choose a number between 0 and 100 representing their perceived risk. These two items were summed for analyses. Internal consistency, as calculated by Cronbach's α, was 0.78.

Self-efficacy. A four-item efficacy scale modeled after Bunn and O'Connor's work (31), measured the individual's level of confidence in (*a*) understanding the genetic basis of colorectal cancer, (*b*) understanding the meaning of the test result for their own health, (*c*) understanding the uncertainty of the MSI test result, and (*d*) understanding the meaning of the test result for their families' health. Items were rated on a five-point Likert scale (1 = not at all confident, 4 = extremely confident). Internal consistency, as calculated by Cronbach's α, was 0.87.

Cancer-Specific Emotional Distress. The Impact of Event Scale—Revised (32), a 22-item questionnaire, was used to assess cancer-specific psychological distress. Items were anchored to worries about colorectal cancer. Items were rated on a four-point Likert scale (1 = not at all, 4 = often). Internal consistency, as estimated by Cronbach's α, was 0.93.

Physician and Family Support for MSI Testing. The physician support measure was adapted from Myers et al. (refs. 33-35) and our previous work with colon cancer screening (22). The scale included two items (e.g., ''I think my doctor wants me to pursue MSI testing''). Items were rated on a four-point Likert scale (1 = strongly disagree, 4 = strongly agree). Cronbach's α was 0.86. The family support measure was adapted from our previous work with colon cancer screening (22). The scale included two items (e.g., ''I think my family wants me to have MSI testing''). Items were rated on a four-point Likert scale (1 = strongly disagree, 4 = strongly agree). Cronbach's α for this scale was 0.73.

Medical Correlates

Medical Information. The date and stage of original colorectal cancer diagnosis, ECOG status, and metastatic status were collected from patients' charts at the time of informed consent.

Family History of Cancer. Participants completed a family history of cancer form. The total number of first- and second-degree relatives with cancer and total number of relatives who died from colorectal cancer were calculated from this form and were included in the analyses.

Results

Descriptive Information Regarding Knowledge about and Media Exposure to MSI Testing. Descriptive information is summarized in Table 2. The level of knowledge about the MSI test was very low. Approximately 43% of the sample participants did not answer any of the items correctly and <20% of participants answered more than half of the items correctly. The average percentage of correct answers was 17.5% (SD = 0.23) and the median percentage of correct answers was 6% (1/14 items). Very few participants had prior media exposure to this test: 98% had never read articles about MSI testing and only 6% had heard about the test on either television, radio, or the Internet.

Descriptive Information Regarding Perceived Benefits and Barriers of MSI Testing. Table 2 presents summary statistics for these variables and Table 3 presents descriptive information on the perceived benefits and barriers of the MSI test. Overall, the benefits of the MSI test were endorsed at a much higher rate than the barriers. The average benefits score was 45.7 (possible range, 14-64) and the average barriers score was 17.62 (possible range, 10-40). Table 3 presents the percentage of participants who reported either ''moderate'' or ''strong'' agreement with each item (Likert rating of ''3'' or ''4''). As can be seen in Table 3, >90% of the sample felt that the MSI test made sense, was convenient, important, and would clarify the participant's personal and family risk for an inherited form of cancer. The highest rated benefit was to learn if one's children and other relatives were at risk for an inherited form of colorectal cancer (98.3%). The only benefit that was not endorsed by the majority of the sample participants was that the results of the MSI test would help the participant with childbearing decisions (28.1%; M_{item} = 1.9).

The level of agreement with MSI barriers was low. As can be seen in the last column of Table 3, the most frequently endorsed barriers (Likert rating of ''3'' or ''4'')

Table 2. Descriptive characteristics for knowledge, psychosocial correlates, and perceived benefits and barriers to MSI testing

Variable	Mean (SD)	Range	Possible range
MSI knowledge	0.18 (0.23)	0-0.82	0-1.00
Media exposure to MSI testing	0.14 (0.34)	0-1	0-1.00
Perceived risk for cancer recurrence	87.61 (46.65)	0-200	0-200
Self-efficacy	7.83 (3.18)	4-16	4-20
Cancer-specific distress	28.63 (17.98)	0-87.6	0-110
Family support for MSI testing	5.83 (1.77)	2-8	2-8
Physician support for MSI testing	6.29 (1.50)	2-8	2-8
Perceived benefits of MSI testing	45.72 (6.22)	25-56	14-56
Perceived barriers of MSI testing	17.62 (5.35)	10-34	10-40

were possible insurance discrimination (32%) and barriers associated with uncertainty associated with the test result: that the MSI test did not provide a definitive answer about inherited colorectal cancer (36.8%), that the test result would not provide proof that the participant had an inherited form of colorectal cancer (34.5%), and that a normal result did not provide definitive proof that the participant did not have an inherited form of colorectal cancer (34.5%).

Associations of Demographic and Medical Factors, MSI Knowledge, Media Exposure, Perceived Risk, Self-efficacy, Distress, and Physician and Family Support with Perceived Benefits, and Barriers of MSI Testing. Table 4 presents the correlations of demographic and medical variables, MSI knowledge, media exposure, perceived risk, self-efficacy, distress, discussion with family about MSI testing, and physician and family support for MSI testing with MSI benefits and barriers. With regard to demographic and medical variables, patients with metastatic disease endorsed fewer benefits from MSI testing [$r = 0.26$; t (124) = -2.99, $P < 0.01$, $M_{\text{metastatic disease}} = 40.93$, $M_{\text{nonmetastatic disease}} = 44.11$]. Higher ECOG status (more difficulty performing activities of daily living) was associated with higher perceived barriers to MSI testing [t (124) = 2.2, $M_{\text{ECOG = 1}} = 19.7$, $M_{\text{ECOG = 0}} = 17.1$].

In terms of associations between knowledge and psychosocial correlates of perceived benefits and barriers, greater perceived risk for cancer recurrence was associated with both significantly fewer perceived benefits and greater perceived barriers to MSI testing. Greater self-efficacy was associated with significantly greater perceived benefits from MSI testing. Cancer-specific distress was associated with higher perceived barriers of MSI testing. Perceived benefits and barriers to MSI testing were significantly, but not highly, correlated with one another.

The next step in the analysis was to evaluate the relative contribution of predictor variables by entering the significant demographic, medical, and attitudinal correlates of perceived MSI benefits and barriers into a predictive model. Because benefits and barriers were not highly correlated and we were interested in determining

Table 3. Descriptive information regarding perceived benefits and barriers of MSI testing

	Mean (SD)	*N* (%)*
Benefits		
Makes sense to me	3.39 (0.65)	116 (92.8)
Easy to do	3.45 (0.62)	115 (92.0)
Important to do	3.51 (0.62)	115 (92.0)
Benefits outweigh difficulties	3.41 (0.70)	108 (86.4)
Would help plan the future	3.10 (0.84)	94 (75.2)
Will give information about risk for another cancer	3.26 (0.81)	102 (81.6)
Help know if have inherited cancer	3.55 (0.64)	115 (92.0)
Want to learn if children and relatives are at risk	3.79 (0.49)	119 (95.2)
Might help with personal worries about another cancer	3.22 (0.86)	99 (79.2)
Help make decisions about medical treatment	3.36 (0.79)	106 (84.8)
Interested in knowing if they have cancer gene	3.55 (0.60)	114 (91.2)
Will give reassurance about inherited cancer risk	3.28 (0.73)	105 (84.0)
Will help make childbearing decision	1.90 (1.09)	34 (27.2)
Doctor thought it was a good idea	3.00 (0.84)	95 (76.0)
Barriers		
Test will not give definitive answer	2.21 (0.82)	43 (34.5)
Abnormal result is not proof of inherited cancer	2.27 (0.83)	46 (36.8)
Normal result is not definite	2.26 (0.83)	43 (34.5)
Do not want to know family CRC risk	1.37 (0.78)	12 (9.6)
Do not want to know personal risk	1.47 (0.80)	17 (13.6)
Too many other stresses	1.54 (0.78)	17 (13.6)
Worried about result	1.65 (0.86)	21 (16.8)
Concerned about family's reactions	1.57 (0.81)	17 (13.6)
Not much can be done about CRC	1.38 (0.73)	10 (8.0)
Concerned about insurance discrimination	1.98 (1.10)	40 (32.0)

*Percentage of participants rating the item on a Likert scale as a ''3'' or a ''4''.

Table 4. Pearson correlations between demographic and medical characteristics, MSI knowledge, psychosocial variables, and perceived benefits and barriers of MSI testing

Variable	Perceived benefits	Perceived barriers
Age	0.07	−0.08
Gender	0.15	−0.01
Income	0.04	−0.06
Education	−0.13	−0.09
ECOG status	−0.06	0.20*
Metastatic status (1 = yes, 2 = no)	0.26 †	−0.08
Time since diagnosis	−0.11	−0.10
Relatives with cancer	−0.04	0.07
Number of relatives who died from CRC	−0.09	0.08
MSI knowledge	0.16	0.09
Media exposure	−0.08	0.18
Perceived risk	−0.22*	0.22*
Self-efficacy	0.30 ‡	−0.07
Cancer-specific distress	0.08	0.25 †
Family support	0.25 †	0.08
Physician support	0.30 †	−0.04
Perceived benefits		−0.22*

*$P < 0.05$.
†$P < 0.01$.
‡$P < 0.001$.

if correlates of motivations differed, separate regression models were created for these variables. The hierarchical multiple regression model included three categories of predictors, entered in hierarchical order/steps: (*a*) demographic variables, (*b*) medical variables, and (*c*) knowledge and attitudinal variables. Only those variables that were significantly associated with each outcome variable in correlational analyses shown in Table 4 were included in each regression equation.

Results of the regression analyses equation predicting perceived MSI benefits are shown in Table 5. The equation did not include any demographic variables and included only one medical variable, metastatic status (yes/no). Knowledge and attitudinal variables entered in the third step included perceived risk for cancer recurrence, self-efficacy, family support for MSI testing, and physician support for MSI testing. In the final model, metastatic status, perceived risk, and self-efficacy were significant predictors of perceived benefits. Physician and family support for MSI testing were no longer significant correlates of perceived benefits. Greater perceived benefits from MSI testing were associated with having nonmetastatic cancer, lower perceived risk for cancer recurrence, and greater self-efficacy. The set of variables accounted for 21% of the variance in perceived benefits.

The results of the regression analyses of factors predicting perceived barriers are shown in Table 5. In the regression equation, there were no demographic variables entered into the equation. In terms of medical variables, ECOG status (coded as a dichotomous variable; 0 versus 1-3) was entered into the equation. There were three knowledge and attitude variables entered into the equation: media exposure, perceived risk for cancer recurrence, and cancer-specific distress. In the final model, only cancer-specific distress was a significant predictor. Greater perceived barriers of MSI testing were associated with greater cancer-specific distress. This set of variables accounted for 14% of the variance in perceived barriers.

Discussion

In this first empirical study evaluating knowledge and attitudes about MSI testing, our primary goal was to characterize the level of knowledge and exposure to this test among individuals at-risk after they were offered the test by their physician. Our results suggested that the vast majority of the samples had very little exposure to, or knowledge about, the purpose and possible outcomes of MSI testing. It is notable that all patients had been introduced to the MSI test by their physician. Despite knowing almost nothing about the test, the participants in our sample held very positive attitudes about the potential benefits and perceived few barriers to undergoing the test. This finding is consistent with previous studies suggesting that individuals hold positive attitudes about mutation testing (18, 23, 36).

The patients' motivations to have MSI testing were similar to those cited by individuals considering other mutation tests. Participants felt that the test would

Table 5. Hierarchical regression model of perceived benefits and barriers of MSI testing (n = 125)

Step	Independent variable	Dependent variables		
		β	R^2	ΔR^2
Perceived benefits				
1	Metastatic disease	0.22*	0.07	0.07
2	Perceived risk	−0.14*	0.21	0.14
	Self-efficacy	0.24 †		
	Family support for MSI testing	0.09		
	Physician support for MSI testing	0.14		
Perceived barriers				
1	ECOG status	0.15	0.04	0.04
2	Media exposure	0.14	0.14	0.10
	Perceived risk	0.16		
	Cancer-specific distress	0.20*		

NOTE: A higher score on metastatic status indicates no metastasis (1 = yes, 2 = no).
*$P < 0.05$.
†P 0.01.

provide information about the inherited risks for their children and other relatives (7, 8). The main difference between the benefits endorsed by individuals considering mutation tests such as the BRCA1/2 test and our sample was that our participants did not perceive that the results of the MSI test would help them with childbearing decisions. However, this finding is likely explained by the fact that the average age of our participants was 44 years old, and future childbearing might no longer be of concern. The primary issues that participants endorsed included insurance discrimination and the uncertainty of test results. Given that the MSI test cannot definitively predict an individual's specific risk for a germ line mutation in MMR genes, uncertainty is a logical concern.

The set of correlates of perceived benefits differed from the set of correlates of perceived barriers. In addition, we were able to account for more of the variance in perceived benefits than perceived barriers, and there were more significant predictors in the regression model predicting perceived benefits. These findings are consistent with elaborations of the Health Belief Model proposed by Ronis (37), who proposed that the Health Belief Model construct of risk predicted perceived benefits rather than perceived barriers. However, we found that greater perceived risk was associated with fewer perceived benefits, which is in contrast with previous findings which have suggested that greater perceived risk for developing a health problem was associated with greater perceived benefits of engaging in the cancer screening (20, 25, 38). Future studies evaluating the role of perceived risk in motivations to undergo genetic screening tests should more thoroughly examine the associations between risk and perceived benefits to having these tests as the associations may differ from other cancer screening practices.

The finding that individuals with nonmetastatic cancer and individuals who perceived themselves at lower risk for cancer recurrence endorsed more benefits suggests that perhaps individuals who were diagnosed with or perceived that they were diagnosed with a less ''threatening'' disease were more motivated to have this test or were able to see its benefits. Patients with more advanced disease are likely dealing with concerns about mortality and might be less able to focus on futuristic issues such as the chance for another primary Lynch syndrome–related cancer or the risk of cancer for other family members. The associations between metastatic status/disease stage and perceived benefits and barriers to genetic testing have not been studied, and therefore, comparisons with previous research cannot be made. However, a related construct, genetic test uptake, has not been significantly associated with disease stage in previous research evaluating factors predicting BRCA1/2 uptake (39). A similar association between lower perceived breast cancer risk and holding positive attitudes about genetic testing is consistent with previous research (19).

Taken together with our finding that greater cancer-specific distress was the only significant correlate of perceived barriers of MSI testing, these results suggest that metastatic disease status, risk perceptions, and patient psychological distress should be taken into account when considering reasons why some individuals formulate their attitudes about whether or not to pursue the MSI test.

The fact that greater self-efficacy or confidence in one's understanding of the MSI test was associated with greater benefits is consistent with the Dual Process Theory, as well as with a wide range of literature suggesting that confidence is a key variable in the ability to make informed decisions about a variety of health behaviors and medical tests (40-42).

It is interesting to note that the highest-rated benefit was learning family member risk for inherited colon cancer; however, family support for MSI testing was not a significant predictor of benefits in the final regression model. It is possible that patients felt obligated to their children and other family members to have this testing done even though they may or may not perceive that they have full family support. This finding might have implications for how the MSI test results and HNPCC test results are eventually communicated to other family members.

Before discussing the clinical implications, the limitations of this study should be considered. First, because participants were being approached for a randomized clinical trial, the amount of information regarding the MSI test, which was provided by the physician before the patient completed the baseline survey, might have differed from normal clinical practice outside of a research study. Because the study team standardized the procedures for referral to the study, patients may have been provided with less information than in normal clinical practice. Second, racial and ethnic minority representation was very low, and our findings might not generalize to non-Caucasian or Hispanic patients. Third, although the study acceptance rate was high, patients who refused participation had lower functional status than study participants, suggesting that our findings may be less generalizable to patients with more functional impairment. This is particularly important because psychological distress and metastatic status were associated with perceived benefits and/or barriers to the MSI test. However, it should be noted that our sample included a high number of patients with metastatic disease.

These findings have clinical implications. Most importantly, patients being offered the MSI test in clinical settings may have little understanding about it or exposure to the topic. In order to make an informed decision, it is important that they be provided with more detailed information about the purposes and outcomes of the test. Second, many patients have concerns regarding possible insurance discrimination and concerns about the uncertainty associated with the test, and should be counseled about these topics prior to making the decision to have the test, particularly considering that this test is the ''gateway'' to further genetic evaluation for HNPCC. Finally, emotional distress and perceived risk for cancer recurrence might color the patients' perceptions of the test in a negative light. Clinicians discussing the test with a more distressed patient may need to address this distress before pursuing the discussion of whether to have the MSI test. Overall, our results point to the importance of educating patients to make a fully informed decision regarding the MSI test. These findings may also have implications for future intervention studies designed to facilitate decisions regarding MSI testing. It may be important to extend intervention content beyond a consideration of perceived benefits and barriers to other factors which may play a role, such as perceived risk for

cancer recurrence, cancer-specific psychological distress, and perceived self-efficacy. We are currently conducting a study to determine whether an educational intervention will affect knowledge, attitudes, and decision-making regarding MSI testing.

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