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Psychological Impact and Associated Factors After Disclosure of Genetic Test Results Concerning Hereditary Nonpolyposis Colorectal Cancer

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1. Introduction

Advances in genetics in recent years have made major contributions to the development of medical genetics. The existence of "familial tumors" has been recognized, and genetic testing, with a potentially incalculable benefit to humanity, is being attempted (Offit, 1998). Numerous gene analyses related to the genesis and development of colorectal cancer have been conducted, and the existence of hereditary colorectal tumors in the form of hereditary nonpolyposis colorectal cancer (HNPCC) and familial adenomatous polyposis (FAP) has been identified.

HNPCC is caused by inherited germline mutations in mismatch repair genes and accounts for 2 -5% of colorectal cancers. The condition is characterized by young-onset, synchronous and metachronous tumors, and a predisposition to gynecologic, urinary tract, and extracolonic gastrointestinal cancers. Genetic testing usually begins with a family member who has been diagnosed with an HNPCC syndrome-related cancer (proband). If a deleterious mutation is identified, testing can be offered to the proband's family members, since they are at risk of carrying the mutation. Knowing one's genetic risk for hereditary cancers may facilitate the early detection or prevention of cancer.

However, in contrast to the advances in scientific techniques, a great deal of apprehension exists with regard to the psychological or ethical, legal, and social issues (ELSI) associated with the application of these techniques. Since important personal genetic information that does not change throughout one's lifetime is handled during genetic diagnosis and an individual's genetic information is partly shared with blood relatives, with the impact of such genetic information not being limited to the individual, we find ourselves in a situation where new life health-care norms that also take psychosocial aspects into consideration are required. For this reason, a variety of studies have been conducted regarding the psychosocial aspects involved in the screening-test-taking behavior of high-risk people, the psychological aspects of high-risk people, interest in genetic counseling and genetic testing, and the psychosocial effects of genetic counseling. Studies on psychosocial aspects after being informed of the test results have also been reported recently, but many of these studies are concerning hereditary breast and ovarian cancer, and very few studies

examining the impact of genetic testing for hereditary colorectal tumors have been performed.

In this article, the psychological consequences related to HNPCC are reviewed with regard to the following four points: (1) attitude toward genetic testing, (2) risk perception, (3) psychosocial effects of genetic counseling, and (4) psychosocial aspects after undergoing genetic testing and being informed of the test results. I have reviewed and selected nearly all the articles regarding these themes using the PubMed database.

2. Attitude toward genetic testing

Many subjects who undergo genetic counseling for HNPCC also wish to undergo genetic testing. However, some subjects refuse to undergo genetic testing, despite its potential benefits. Some previous studies investigated the relationships between the intention to undergo genetic testing and psychosocial variables.

Hadley et al. (2003) investigated attitudes, intention, and the completion of genetic testing among 111 newly identified family members (first-degree relatives) of individuals with HNPCC. Most (97%) stated their intention to pursue testing. Fifty-one percent reported that learning about their children's risks was the most important reason to consider testing. The participants' intentions to pursue genetic testing were significantly affected by concerns regarding their ability to handle the emotional aspects of testing and the psychosocial effect on family members. On the other hand, 39% identified the potential effect on their health insurance as the most important reason not to undergo testing.

Wakefield et al. (2007a) qualitatively assessed 22 individuals' attitudes toward genetic testing for HNPCC. The most frequently reported pros were "to help manage my risk of developing cancer", "to help my family", and "to know my cancer risk." The participants expressed concern about the potential psychological impact of genetic testing. The authors also found that some affected individuals may not fully comprehend the meaning of their potential test results.

Wakefield et al. (2008) conducted a randomized trial to measure the effectiveness of a tailored decision aid designed specifically to assist individuals to make informed decisions regarding genetic testing for HNPCC. The decision aid explains the evidence available regarding HNPCC-related cancer risks, the differences between a mutation search and predictive testing, and the potential benefits, risks, and limitations of testing (Wakefield et al., 2007b). One hundred and fifty-three individuals were randomly assigned to a group who received the decision aid or a group who received a control pamphlet. Evaluations were conducted 1 week after consultation and 6 months after the completion of the intervention using a questionnaire, and 95 subjects completed the 6-month follow-up questionnaire. Although the decision aid had no significant effect on the actual genetic testing decision, the participants who received the decision aid had significantly lower levels of decisional conflict regarding genetic testing and were more likely to be classified as having made an informed choice concerning genetic testing than participants who received a control pamphlet. Furthermore, men who received the decision aid had significantly higher knowledge levels regarding genetic testing than men who received a control pamphlet.

These reports suggest that most individuals pursue genetic testing to help manage their own risk of developing cancer and to learn about their children's risks. On the other hand,

however, concerns about psychological and psychosocial issues may present barriers to undergoing genetic testing. The development of patient education tools, such as the decision aid, is needed.

3. Risk perception

HNPCC mutation carriers have a life-time risk of colorectal cancer of about 80%, while female carriers have a 40-60% risk of endometrial cancer and a 10-15% risk of ovarian cancer. Communicating cancer risk and assessing the perceived risk is very important for genetic counseling because of subsequent cancer prevention behavior or cancer-related distress. Four reports were extracted regarding risk perception among individuals at risk for HNPCC.

Codori et al. (2005) assessed the effect of genetic counseling on perceived lifetime risk and cancer-distress among 101 adult first-degree-relatives of colorectal cancer patients from families with known or suspected HNPCC. Most persons overestimated their cancer risk, and a higher perceived risk was associated with believing that colorectal cancer cannot be prevented. The individual perceived risk changed after counseling, although the mean perceived risk was unchanged.

Domanska et al. (2007) investigated the perceived cancer risk among 47 HNPCC mutation carriers and correlated the findings with individual characteristics. A perceived risk of colorectal cancer above 60% was reported by 49% individuals, and only one reported a perceived risk > 80%. Female mutation carriers, individuals under the age of 50 years, and individuals who received their counseling within 1 year prior to the study reported a higher perceived risk of colorectal cancer. Individuals who had lost a parent to HNPCC-related cancer at an early age also reported a higher perceived risk. Regarding gynecological cancer, 33% of the women reported a perceived risk of 40-60% for endometrial cancer, whereas the remaining 67% either underestimated or overestimated their risk.

van Oostrom et al. (2007) studied the difference in cancer risk perception among 271 individuals who opted for genetic cancer susceptibility testing for a known familial BRCA1/2 or HNPCC related germline mutation. The assessment was conducted before, 1 week after, and 6 months after disclosure of the test results. Individuals from BRCA1/2 and HNPCC mutation families did not differ with regard to their risk perceptions over time. Individuals from BRCA1/2 families perceived hereditary cancer as being more serious.

Grover et al. (2009) examined colorectal cancer risk perception among individuals tested for mismatch repair genes mutation and identified factors associated with an appropriate interpretation of their cancer risk. In this study, in particular, the authors paid attention to individuals with an indeterminate genetic test result. Pathogenic mutations in *MLH1* and *MSH2* have been identified in only 30% to 64% of families who meet the clinical criteria for HNPCC and have undergone testing. Genetic testing may not yield a definitive result because of the lack of an identifiable mutation in one of the known genes or a mutation of unclear pathogenic significance. In the absence of an identified family mutation, these results are considered indeterminate or uninformative. Patients remain at an increased risk for colorectal cancer, and intensive cancer screening recommendations are made based on their personal and family cancer histories. A total of 159 individuals who met the Revised Bethesda Guidelines and had previously undergone genetic testing participated in this study. Ninety individuals with a pathogenic mutation (true positive) correctly estimated their cancer risk. However, only 62% of individuals with an indeterminate genetic test result

correctly estimated their risk. Individuals with a history of HNPCC-associated cancer or indeterminate genetic test results were significantly less likely to estimate their cancer risk as being increased.

These reports suggest that despite educational efforts and an increasing amount of data on the risk of cancer associated with HNPCC, few individuals report a perceived risk that is actually correct. In particular, individuals at risk for HNPCC who receive an indeterminate genetic test result may be falsely reassured. It is important that health care providers continue to device a counseling approach for promoting a correct understanding of cancer risk and for discussing the implications of uninformative results on the lifetime cancer risk.

4. Psychosocial effects of genetic counseling

Cancer genetic counseling has become popular as a result of the recent development of genetic tests that pinpoint familial cancer risk. Such counseling is composed of presymptomatic risk assessment and management (cancer risk counseling) and reproductive risk counseling. The former has two components: risk assessment and counseling regarding behavioral, medical, and surgical options to decrease risk. A basic goal of cancer risk counseling is to derive and explain an individual's cancer risk in clear terms, and the counselor's role is to educate and enumerate options for patients and clinicians, answer questions regarding what is known, and suggest appropriate referrals to help individuals reach difficult decisions.

A cancer risk counseling session is comprised of the following components: 1) baseline risk perception; 2) medical history and exposure history; 3) pedigree construction and pedigree documentation; 4) empiric risk assessment and genetic risk assessment; 5) options for early detection and prevention; 6) options, risks, and benefits of genetic testing; and 7) response to questions, support, and plans for follow-up. Throughout these discussions, a sensitivity to the psychological and ethical aspects of counseling is essential. Therefore, continued follow-up by the counselor after the session is the best way to limit the potential for adverse effects as a result of the knowledge of an inherited cancer risk, and ready access to liaison mental health professionals with experience in cancer genetics is thought to be a valued asset of cancer risk counseling.

Psychological research on aspects of cancer genetic counseling has focused on three broad areas: factors predicting interest in cancer genetic testing (Lerman et al., 1996), the psychological impact and effect of genetic counseling and testing for inherited cancer risk (Lerman et al., 1997), and the relationship between psychological distress and preventive behaviors (Kash et al., 1992). In each of these areas, the results have implications for the management of at-risk individuals. However, such data is unlikely to be applicable to every case because of cultural differences among study populations and the complexity of the instruments used in research studies, in addition to the fact that most of these studies have been performed for hereditary breast cancer. In this section, four studies on the psychological impacts of genetic counseling regarding HNPCC are reviewed.

Keller et al. (2002) explored distress before and after comprehensive interdisciplinary counseling in families at risk for HNPCC. Sixty-five individuals (31 patients with colorectal cancer and 34 unaffected at-risk persons) participated in this study. Data were collected from semi-structured questionnaires before, as well as 4-6 weeks after counseling. Distress declined after counseling, as did worries related to HNPCC. A trend toward a greater anticipated ability to cope with a positive gene test was also observed after counseling. Changes after counseling were generally more pronounced for persons at risk, compared

with those for patients with cancer. A substantial minority, however, said that they experienced increased worry and physical symptoms after counseling.

Bleiker et al. (2007) examined: 1) levels of cancer-specific distress more than one year after genetic counseling for HNPCC; 2) associations between sociodemographic, clinical and psychosocial factors and levels of distress; 3) the impact of genetic counseling on family relationships; and 4) the social consequences of genetic counseling. One hundred and sixteen individuals who participated in this study completed a self-report questionnaire by mail an average of 4 years after the last counseling session. Among all the subjects, 6% had clinically significant levels of cancer-specific distress (Impact of Event Scale). Having had contact with a professional psychosocial worker for cancer risk in the past 10 years was significantly associated with higher levels of current cancer specific distress. Only a minority of the subjects reported any adverse effects of genetic counseling on communication regarding genetic counseling with their children, family relationships, obtaining life insurance, choice or change of jobs, and obtaining a mortgage.

Keller et al. (2008) conducted a prospective study that examined the impact of multidisciplinary risk counseling on the psychosocial outcome of 139 affected cancer patients and 233 family members without cancer but at risk for HNPCC. Participants completed questionnaires specific to HNPCC before and 8 weeks after attending the cancer clinic. The levels of distress among affected patients exceeded those of unaffected individuals, as did worry regarding their relatives' risk. A significant reduction in general anxiety (Hospital Anxiety and Depression Scale), distress specific to familial colorectal cancer (Impact of Events Scale), and general cancer worry (Distress due to Hereditary Disorder) was demonstrated after counseling among both the affected patients and unaffected individuals. The reduction in distress was more pronounced among affected patients given a high risk of HNPCC than among those with an intermediate risk.

Hasenbring et al. (2011) prospectively examined the impact of an initial interdisciplinary genetic counseling on feelings of anxiety with a special focus on subgroups related to personal cancer history, sex, age, and education. A significant interaction between time, sex, and age was identified for change in anxiety. While women in general and men older than 50 years revealed a significant reduction in anxiety, younger men did not show any change over time. A logistic regression analysis indicated that clinical Hospital Anxiety and Depression Scale-A cases could be predicted based on general distress (Brief Symptom Inventory) as well as by HNPCC-related cognitions of intrusion and avoidance (Impact of Event Scale) with a correct classification of 86%.

These studies indicate that anxiety and cancer-specific distress are reduced after genetic counseling, suggesting an overall beneficial impact of comprehensive counseling. On the other hand, a minority of individuals, such as cancer-affected younger men, exhibited adverse effects of genetic counseling on psychosocial variables. Thus, healthcare providers (genetic counselors, human geneticists, oncologists, and psycho-oncologists) should always be aware of psychosocial issues after genetic counseling. However, as little data is available on the psychosocial effects of genetic counseling regarding HNPCC, further data accumulation is needed.

5. Psychosocial aspects after being informed of genetic test results

Since 1991, when a gene for hereditary cancer was first identified, studies expressing concern about the psychosocial aspects of gene diagnosis began in Western countries, with

the results starting to be reported in 1993. Although studies investigating psychosocial aspects after the subjects had undergone actual genetic testing and had been informed of the test results have been reported, many of these studies have concerned hereditary breast and ovarian cancer, and only a few studies have been performed for HNPCC. Furthermore, little is known about the factors associated with psychosocial aspects. However, HNPCC testing might offer more benefit than hereditary breast and ovarian cancer testing because of the differences in the risk management options available to mutation carriers. In HNPCC, a colonoscopy every 1–2 years is more effective for detecting and preventing adverse health outcomes than measures available to carriers of hereditary breast and ovarian cancer mutations. Therefore, identifying the psychosocial situations in which individuals at risk for colorectal cancer have lived after the disclosure of genetic information or the way in which healthcare providers are able to support the mental states of these individuals are important.

Ten original articles (review articles were not included) assessing psychosocial aspects after individuals had been informed of genetic test results regarding HNPCC were extracted. In this chapter, cross-sectional studies that assessed psychosocial aspects at one time point after disclosure and prospective studies that followed-up psychosocial aspects for 1 year or longer after disclosure are described separately. A summary is shown in Table 1.

5.1 Cross-sectional studies assessing psychosocial aspects after the subjects had been informed of the test results

Four articles were extracted. Esplen et al. (2001) investigated psychosocial function in 50 individuals who were engaged in the genetic test process for HNPCC (the period between the psychosocial assessment and the disclosure of the test results was 1 – 48 months). Twenty-three individuals were identified as carriers (13 had a previous history of CRC), seven were non-carriers and 20 individuals were still awaiting their test results. The psychosocial scores demonstrated that a subgroup of individuals exhibited distress, with greater distress for those individuals awaiting results or testing positive. A high level of satisfaction was associated with the experience of testing.

Claes et al. (2004) assessed the short-term impact (1month after test result disclosure) of genetic testing using a semi-structured interview and self-reported questionnaires. The subjects were 40 cancer-unaffected relatives who had undergone predictive testing for HNPCC. Distress was within the normal ranges. Distress decreased significantly from pre- to post-test in non-carriers but not in carriers.

Murakami et al. (2004) identified the prevalence rates and predictors of psychological distress and evaluated the feelings of guilt at one month after the disclosure of test results in Japanese probands and unaffected relatives. The prevalence of major and minor depression, acute stress disorder (ASD), posttraumatic stress disorder (PTSD), and posttraumatic stress symptoms (PTSS) were assessed using the Structured Clinical Interview based on the Diagnostic and Statistical Manual of Mental Disorders, 3rd edition revised (DSM-III-R) or the DSM-IV; feelings of guilt were investigated using a numeric scale and a semi-structured interview. Forty-two participants completed the 1-month follow-up interview. Although none of the participants met the criteria for major depression, ASD, or PTSD at the time of the follow-up interview, 7% of the participants met the criteria for minor depression and 5% had PTSS. The only predictor of psychological distress was the presence of a history of major or minor depression. Twelve percent of the participants had feelings of guilt.

Author, year	Subjects	Study design	Assessment period after disclosure	Study method / outcome measures	Main study findings	Associated factors
Esplen et al, 2001	50 affected and unaffected individuals	Cross-sectional	1 – 48 months	Questionnaires / CES-D, IES, STAI	The psychosocial scores demonstrated that a subgroup of individuals exhibited distress, with greater distress for those individuals awaiting results or testing positive.	Disclosure their test results to family and non-family members
Aktan-Collan et al, 2001	271 unaffected individuals	Prospective	1 and 12 months	Questionnaires / STAI	The mutation-positive subjects were more anxious than their counterparts immediately after the test disclosure, but the differences had disappeared at the follow-ups. In other variables, neither differences between the groups defined by mutation status nor changes with time were detected.	Not shown
Claes et al, 2004	40 unaffected individuals	Cross-sectional	1 month	Questionnaires / SCL-90, STAI	Distress was within normal ranges. Distress decreased significantly from pre- to post-test in non-carriers and did not in carriers.	Not shown
Murakami et al, 2004	42 affected and unaffected individuals	Cross-sectional	1 month	Semi-structured interview / major depression, minor depression, ASD, PTSD, PTSS, guilt	Although none of the participants met the criteria for major depression, ASD, or PTSD at the follow-up interview, 7% of participants met the criteria for minor depression and 5% had PTSS. Twelve percent of participants had feelings of guilt.	Presence of history a major depression

Table 1. (continued)

Meiser et al, 2004	40 unaffected individuals	Prospective	2 weeks, 4 months and 12 months	Questionnaires / HADS, IES, STAI	Carriers showed a significant increase in mean scores for intrusive and avoidant thoughts 2 weeks and a significant decrease in mean depression scores 2 weeks and 4 months. For non-carriers, significant decreases in mean scores for intrusive and avoidant thoughts, depression scores and mean state anxiety scores were observed at all follow-up assessment time points.	Not shown
Gritz et al, 2005	155 affected and unaffected individuals	Prospective	2 weeks, 6 months and 12 months	Questionnaires / CES-D, IES-R, QLI, STAI	Mean scores on all outcome measures remained stable and within normal limits for cancer-affected participants. Among unaffected carriers, mean depression and state anxiety scores increased from baseline to 2 weeks and decreased from 2 weeks to 6 months. Among unaffected non-carriers, mean depression and anxiety scores did not differ..	Baseline mood disturbance, lower quality of life, and lower social support
Claes et al, 2005	72 unaffected individuals	Prospective	1 month and 12 months	Questionnaires / IES, SCL-90, STAI	Mean levels of distress (cancer-specific distress, state anxiety, psychoneuroticism) were within normal ranges and none of the participants had an overall pattern (on all scales) of clinically elevated levels of distress.	Not shown

Table 1. (continued)

Collins et al, 2007	73 unaffected individuals	Prospective	2 weeks, 4 months, 1 year, and 3 years	Questionnaires / HADS, STAI, IES-R	Mean cancer-specific distress in carriers increased at 2 weeks with a return to baseline levels by 12 months. This level was maintained until 3 years. Non-carriers showed sustained decreases after testing with a lower level at 3 years compared with baseline. Mean depression and anxiety scores did not differ between carriers and non-carriers and, at 3 years, were similar to baseline.	Not shown
Yamashita et al, 2008	46 affected and unaffected individuals	Cross-sectional	1 month	Questionnaires / IES-R	Comparison of the IES-R scores showed that they tended to be higher in the mutation-positive group, but the differences were not statistically significant.	Personality tendency "nervousness", Verbal memory
Shiloh et al, 2008	253 affected and unaffected individuals	Prospective	6 months and 12 months	Questionnaires / CES-D, IES-R	Mean reductions were indicated in distress and depression levels within the first 6 months after testing. The interaction between time and mutation was neither significant for distress nor for depression.	Coping style (high monitors)

CES-D: Center for Epidemiological Studies-Depression, IES: Impact of Event Scale (IES-R: Impact of Event Scale-Revised), HADS: Hospital Anxiety and Depression Scale,
QLI: Quality of Life Index, SCL-90: Symptom Checklist, STAI: State-Trait Anxiety Inventory
ASD: acute stress disorder, PTSD: post-traumatic stress disorder, PTSS: post-traumatic stress symptoms

Table 1. Characteristics of studies on psychosocial aspects and associated factors after being informed of genetic test results regarding HNPCC

Yamashita et al. (2008) elucidated the psychological impact at one month after the disclosure of genetic test results regarding HNPCC and assessed the associated factors, focusing on memory function in particular. The subjects were persons who were suspected of having HNPCC and had been given the choice of undergoing genetic testing. The post-genetic testing psychological impact was evaluated using the Impact of Event Scale-Revised (IES-R), and personality tendencies and memory function were evaluated. Final data were obtained from 46 Japanese probands and unaffected relatives (mutation-positive in 18 subjects, uninformative in 18 subjects, and mutation-negative in 10 subjects). A comparison of the IES-R scores showed that they tended to be higher in the mutation-positive group, but the differences were not statistically significant. The personality tendency "nervousness" and the verbal memory assessed prior to disclosure were significantly associated with the total IES-R score.

5.2 Prospective studies assessing psychosocial aspects after the subjects had been informed of the test results

Six articles were extracted. Aktan-Collan et al. (2001) assessed general anxiety, fear of cancer and death, satisfaction with life, and attitude regarding the future using a questionnaire survey in 271 individuals with no personal cancer history who were tested for HNPCC. Measurements were made before the first counseling (baseline), at the test disclosure session, and 1 and 12 months after disclosure. Although the mutation-positive individuals were more afraid of cancer than those who were mutation negative at every measurement point, the fear of cancer decreased significantly from the baseline until after disclosure in both groups. The mutation-positive subjects were more anxious than their counterparts immediately after the test disclosure, but the differences had disappeared at the follow-up examinations. Regarding the other variables, no differences among the groups defined according to mutation status or changes over time were detected.

Meiser et al. (2004) assessed the psychological impact of predictive genetic testing for HNPCC in 114 individuals with no personal cancer history (32 carriers and 82 non-carriers) using mailed self-administered questionnaires prior to and 2 weeks, 4 months and 12 months after the disclosure of the test results. Compared with the baseline results, carriers showed a significant increase in the mean scores for intrusive and avoidant thoughts regarding colorectal cancer at 2 weeks after test result disclosure and a significant decrease in the mean depression scores at 2 weeks and 4 months after test result disclosure. For non-carriers, significant decreases in the mean scores for intrusive and avoidant thoughts regarding colorectal cancer were observed at all follow-up assessment time points relative to the baseline. Non-carriers also showed significant decreases from the baseline in the mean depression scores at 2 weeks, 4 months and 12 months after test result disclosure. Significant decreases in the mean state anxiety scores from the baseline were also observed for non-carriers at 2 weeks after test result disclosure.

Gritz et al. (2005) examined the impact of HNPCC genetic test results on the psychological outcomes of cancer-affected and -unaffected participants up to 1 year after test result disclosure. A total of 155 persons completed the study measures before HNPCC genetic testing and at 2 weeks and 6 and 12 months after the disclosure of the test results. The mean scores for all the outcome measures remained stable and within the normal limits for cancer-affected participants, regardless of the mutation status. Among unaffected carriers of HNPCC-predisposing mutations, the mean depression, state anxiety, and cancer worry scores increased from baseline to 2 weeks after test result disclosure and decreased from 2 weeks to 6 months after test result disclosure. Among unaffected non-carriers, the mean depression and anxiety scores did not differ, but the cancer worry scores decreased during

the same time period. Affected and unaffected carriers had higher mean test-specific distress scores at 2 weeks after test result disclosure, compared with non-carriers, in their respective groups; the scores decreased for affected carriers and all unaffected participants from 2 weeks to 12 months after test result disclosure. Higher levels of baseline mood disturbance, a lower quality of life, and lower social support were associated with a risk for both short- and long-term increases in distress.

Claes et al. (2005) evaluated distress one year after the disclosure of a predictive genetic test result for HNPCC in 72 cancer-unaffected relatives (36 carriers and 36 non-carriers). The mean levels of distress (cancer-specific distress, state anxiety, and psychoneuroticism) were within the normal ranges and none of the participants had an overall pattern (on all scales) of clinically elevated levels of distress. Carriers had significantly higher cancer-related distress one year after test result disclosure than non-carriers. In both groups, colorectal cancer-related distress decreased. Non-carriers additionally showed decreased endometrial cancer-related distress and state anxiety.

Collins et al. (2007) conducted a 3-year study of individuals who received predictive genetic test results for previously identified familial mutations regarding HNPCC. Questionnaires were sent before attendance and 2 weeks, 4 months, 1 year, and 3 years after receiving the test results. Psychological measures were included each time. The study included 73 individuals with no personal cancer history (19 carriers and 54 non-carriers). The results showed an increase in mean cancer-specific distress in carriers at 2 weeks with a return to baseline levels by 12 months. This level was maintained until 3 years. Non-carriers showed sustained decreases after testing with a significantly lower level at 3 years compared with at baseline. These scores tended to be lower than those for carriers at 3 years. The mean depression and anxiety scores did not differ between carriers and non-carriers and, at 3 years, were similar to the baseline scores.

Shiloh et al. (2008) assessed the emotional effects of genetic testing for HNPCC at baseline before testing and again at 6 and 12 months after testing. The subjects were 253 cancer-affected and -unaffected individuals. Negative emotional reactions were evaluated using the Revised Impact of Event Scale and the Center for Epidemiological Studies-Depression Scale. Monitoring coping style was assessed at baseline using the Miller Behavioral Style Scale. Mean reductions were indicated in distress and depression levels within the first 6 months after testing. High monitors (individuals who vigilantly attended to threatening cues in their environment in an attempt to emotionally process the situation and who actively engaged in information seeking and cognitive problem solving with the intention of taking precautions) were generally more distressed than low monitors, specifically if they had indeterminate or positive results.

5.3 Summary

Many studies have shown that genetic testing does not result in short- or long-term significant adverse psychological outcomes, including depression, anxiety, and posttraumatic stress disorder (PTSD), in either carriers or non-carriers or in either cancer-affected or cancer–unaffected individuals. However, healthcare providers should assess psychological responses, such as minor depression, posttraumatic stress symptoms (PTSS), and feelings of guilt, particularly in individuals who have a history of major or minor depression, nervous personality tendencies, baseline mood disturbances, a lower quality of life, or lower social support.

Lastly, two cases that showed adverse psychological reactions after being informed of genetic test results will be presented. The first case is a man who was diagnosed as having

acute stress disorder at a 1-month follow-up examination after the disclosure of a genetic test result, despite the fact that the test result had been negative. The second case is a man who felt guilty after hearing of the positive test results of family members of individuals belonging to his support group.

5.4 Cases exhibiting adverse psychological reactions

[Case 1] Mr. A was a 39-year-old married man without children who came for genetic counseling and testing because of a family history of colon cancer. He had no history of cancer, but his father had a history of colon cancer and his sister had died of the disease at an early age. To confirm the diagnosis of HNPCC, a blood sample was obtained and mutations in the hMSH2 and hMLH1 genes were analyzed. He then consented in writing to participate in our study, and a baseline interview was conducted. He did not meet any of the criteria for any psychiatric disorders.

Approximately two months after the blood test, he underwent post-test counseling and was informed that no mutations had been detected in either the hMSH2 or hMLH1 gene. Four weeks after the disclosure of the test result, at a 1-month follow-up examination, he was diagnosed as having acute stress disorder according to a structured clinical interview based on the DSM-IV. The total score of the Impact of Event Scale-Revised was high. The score for Total Mood Disturbance in the Profile of Mood States was higher than that at the baseline interview. He reported that although he felt emotional relief to learn the negative result, his worries regarding colon cancer had increased instead of disappearing.

Mutation-negative individuals often choose not to participate in follow-up counseling after genetic testing. However, this case suggests that it is important to evaluate the psychological outcome after genetic testing regardless of the test result, and that psychiatrists or psychologists should support the genetic counseling system.

[Case 2] Mr. B, a 59-year-old man, underwent a total colectomy for the resection of colorectal cancer. He and his 25-year old son requested predictive genetic testing 3 years later to reduce uncertainty and to help plan his son's future, since Mr. B's mother had died of colon cancer secondary to HNPCC. Mr. B and his son were provided with both an educational session explaining the genetics of hereditary diseases and counseling regarding the possible impact of positive test results. The tests revealed the presence of a mutation in the father but not in the son. Mr. B was relieved that his "bad blood" had not been passed on to his son. Later, however, he began to experience anhedonia and became depressed for several days. His primary care physician could not determine the reason for his feelings.

Mr. B was the chairperson of a hereditary cancer patient support group run by patients, their families, and health care providers. The group had been established to help families with hereditary cancer exchange information and experiences. Mr. B began to feel guilty because his son had tested negative while the family members of others in his support group had tested positive for the disease.

6. Conclusion

Cancer genetic counseling and genetic testing for HNPCC are now conducted in ordinary clinical settings. However, as mentioned above, few studies have examined the psychosocial aspects of genetic testing for HNPCC, and psychosocial assessments and long-term follow-up care for individuals who have undergone genetic counseling or testing and at-risk relatives with no personal history of cancer remain insufficient. To develop this field, the following problems should be examined: 1) the development of a cancer genetic counseling

model, including psychosocial support; 2) the education of cancer genetic counselors; 3) the availability of appropriate information concerning cancer genetics; 4) the recruitment of subjects at risk for cancer susceptibility; and 5) the accumulation of further psycho-oncology research results. While it is by no means easy to deal with these problems, it is essential that medical oncologists, surgical oncologists, psycho-oncologists, medical geneticists, nurses, and all other health care providers involved in cancer care vigorously approach this new area in collaboration with one another.

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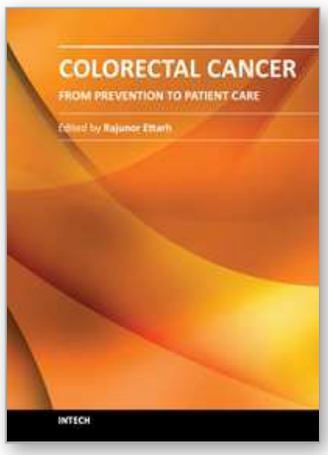

Colorectal Cancer - From Prevention to Patient Care
Edited by Dr. Rajunor Ettarh

ISBN 978-953-51-0028-7
Hard cover, 538 pages
Publisher InTech
Published online 17, February, 2012
Published in print edition February, 2012

The projections for future growth in the number of new patients with colorectal cancer in most parts of the world remain unfavorable. When we consider the substantial morbidity and mortality that accompanies the disease, the acute need for improvements and better solutions in patient care becomes evident. This volume, organized in five sections, represents a synopsis of the significant efforts from scientists, clinicians and investigators towards finding improvements in different patient care aspects including nutrition, diagnostic approaches, treatment strategies with the addition of some novel therapeutic approaches, and prevention. For scientists involved in investigations that explore fundamental cellular events in colorectal cancer, this volume provides a framework for translational integration of cell biological and clinical information. Clinicians as well as other healthcare professionals involved in patient management for colorectal cancer will find this volume useful.

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