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Appraisal of Emerging Symptoms of Colorectal Cancer: Associations with Dispositional, Demographic, and Tumor Characteristics

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Abstract

The time it takes for individuals to realize that their emerging colorectal cancer (CRC) symptoms are serious is often an impediment to expeditious help-seeking. Tailored educational efforts to hasten symptom appraisal time would benefit from knowledge of the characteristics of individuals who tend to neglect their symptoms as well as the nature of symptoms that are most often neglected. In a sample of 112 CRC patients, we investigated associations between duration of symptom appraisal and: (1) trait anxiety, and (2) tumor location, which affects symptomatology. Symptom appraisal duration was associated with a sex-by-anxiety interaction ($p = 0.007$). The longest times (in weeks) were among *high* anxiety females (*Mdn* = 26.0) and *low* anxiety males (*Mdn* = 17.0), with shorter times among *low* anxiety females (*Mdn* = 9.0) and *high* anxiety males (*Mdn* = 2.0). Symptom appraisal times were also longer for patients with distal (vs. proximal) tumors ($p = 0.036$).

Keywords

colorectal cancer; symptom appraisal; trait anxiety; sex differences; Common-Sense Model

Introduction

Colorectal cancer (CRC) is currently the fourth deadliest cancer worldwide (Ferlay et al., 2010), a reality that stands in stark contrast to the fact that CRC is usually curable when diagnosed early, at the localized stage (American Cancer Society, 2011). But achieving widespread early detection and diagnosis of CRC has been a challenge. For example, even

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though it is clear that routine screening is the most effective way to detect CRC at the localized stage, screening rates among eligible adults are far from desirable (Howard et al., 2009). As a result, a substantial proportion of people who develop CRC are not diagnosed until after symptoms appear, thus increasing the chance that they will be diagnosed with more advanced disease than if the CRC had been detected by screening. Furthermore, even if a person does begin to experience symptoms of CRC, he or she may not always react by seeking expeditious medical evaluation. In fact, in a review of several empirical studies, the median length of time reported between CRC symptom onset and the first consultation with a doctor about those symptoms ranged up to 5 months. The authors of the review referred to this period of time as “patient delay” (Mitchell et al., 2008).

Although asymptomatic screening should be promoted as the first line of defense against CRC, education about what to do if symptoms begin should also have a place in the early detection armamentarium. For educational efforts to be most effective, however, it is first necessary to understand where deterrents to timely help-seeking are most likely to occur along the trajectory from symptom onset to appropriate medical treatment. To facilitate that understanding, researchers have conceptualized the total time period from onset of cancer symptoms to initiation of treatment as a series of distinct time intervals, each interval having its own unique characteristics (Andersen et al., 1995). Recently, this time intervals approach has been refined and formalized in “The Aarhus Statement,” a document prepared by an international Consensus Working Group (CWG). The goal of this group was to “formulate definitions of key time points and to make methodological recommendations for researchers” (Weller et al., 2012). The four key time points they identified are: (1) date of first symptom, (2) date of first presentation (typically to a primary care provider or clinic), (3) date of referral (from the primary care provider or clinic to a specialist), and (4) date of diagnosis. In addition, the CWG recommended labels for the intervals spanning these time points. For example, the total time period from date of first symptom until date of first presentation was designated the “patient interval,” because this is the time during which patients have primary control over the decisions that are made and the actions that are taken with respect to seeking medical attention. (It should be noted that the “patient interval” is equivalent to the time period labeled “patient delay” in the review by Mitchell et al. [2008], although the Aarhus CWG advocated changing the terminology). Similarly, the Aarhus CWG labeled the time period between date of first presentation and date of diagnosis as the “diagnostic interval.” This is the time during which the primary care provider assesses the patient’s symptoms and makes a referral, and the diagnosis of CRC is made.

In order to gain a deeper understanding of the unfolding of events prior to a person’s seeking help for his or her symptoms, the total “patient interval” was further divided by the Aarhus CWG into two sequential component intervals: (1) the “symptom appraisal interval” and (2) the “help-seeking interval.” The “symptom appraisal interval” begins when a person first notices unusual bodily changes and ends when he or she determines that those bodily changes could be signaling an important medical problem. This interval represents the time during which a person compares his or her symptoms to knowledge of possible diseases or conditions that might explain the symptoms (Cacioppo et al., 1986; Leventhal et al., 2003; Leventhal et al., 2011). The “help-seeking interval” begins with a person’s recognition that his or her bodily changes are most likely signaling a significant medical problem and ends

when that person has made their first contact with a health care provider for professional evaluation of their symptoms. This interval is thus characterized by a person's consideration and pursuit of different courses of action aimed at getting medical help (Weller et al., 2012).

Important insights have been gained using the time intervals approach. For example, by asking cancer patients to estimate the respective lengths of the symptom appraisal and help-seeking intervals, several researchers have demonstrated that – on average – the symptom appraisal interval accounts for 60–70% of the total patient interval (e.g., Andersen et al., 1995; Cacioppo et al., 1986; Ristvedt & Trinkaus, 2005). In other words, most of the time prior to seeking help for symptoms of a potentially fatal disease is spent with persons believing that their symptoms are not serious and thus not in need of medical attention.

Knowing that the symptom appraisal interval represents the time during which the longest delays are most likely to occur raises further important questions. For instance, do the individuals who demonstrate the most protracted symptom appraisal times share any personal characteristics that could help to explain why they take so much longer than others to realize that their symptoms are serious? A second question that is raised is this: Are there certain kinds of symptoms that are more likely to be neglected than other kinds of symptoms? Developing CRC can first become apparent in a variety of ways, often depending upon where the tumor lies along the length of colon, with initial symptoms ranging from rectal bleeding and changed bowel habits to abdominal pain and fatigue (Majumdar et al., 1999). So, the focus of education should be on providing information about those symptoms that are most likely to be misattributed to benign causes. Answers to questions such as the two listed here could greatly assist in the crafting of informational interventions designed to quicken help-seeking for symptoms of CRC. The most impactful interventions would take into account the characteristics of the most appropriate recipients of those interventions as well as the content of the information that is most important to convey.

The Present Study

The purpose of this study was to elucidate factors associated with length of symptom appraisal time in CRC. The conceptualization of the study may be best understood within the theoretical framework of the common-sense model (CSM) of self-regulation, which has been developed over the past few decades as a model for understanding psychological and behavioral processes involved in the management of everyday health threats (Leventhal et al., 2003; Leventhal et al., 2011). According to CSM, the very first step in the care-seeking process is the initial detection of deviations from one's prototypical physical functioning (Cameron et al., 1993). It is at that point that the affected person begins construction of an "illness representation," which is a cognitive representation that combines his or her somatic perceptions (e.g., rectal bleeding, abdominal pain, fatigue) with the abstract concepts elicited by those perceptions (e.g., hemorrhoids, stress, cancer) (Leventhal et al., 2003). It is important to note that illness representations are shaped over time in a dynamic process as somatic perceptions, abstract concepts, and the associations between the two evolve. In the context of CSM, duration of the symptom appraisal interval may be viewed as the length of time that it takes the person to arrive at an illness representation that crosses the line from

benign to potentially serious and that suggests an action plan for managing the illness threat (Leventhal et al., 2003; Leventhal et al., 2011).

In this study, particular attention was given to two factors that could impact the symptom appraisal process: (a) patient dispositional characteristics and (b) tumor location, which is closely associated with the types of symptoms that occur. With respect to dispositional characteristics, we specifically considered trait anxiety, which may be viewed as a measure of individual differences in sensitivity (or responsiveness) to personally threatening information. Furthermore, anxiety has been recognized as playing a central role in the construction of illness representations and in the management of health threats, according to CSM (Cameron, 2003). Interestingly, in a previous study of recently diagnosed rectal cancer patients, symptom appraisal time was significantly associated with an interaction between sex and trait anxiety. In contrast to females, for whom no significant association was found between trait anxiety and symptom appraisal time, males who were low in trait anxiety reported having taken inordinately longer to recognize their symptoms were serious (*Mdn* = 13.0 weeks) as compared to males who were moderate (*Mdn* = 3.0 weeks) or high (*Mdn* = 2.5 weeks) in trait anxiety (Ristvedt & Trinkaus, 2008). One interpretation of this finding is that a particular subset of males who have low levels of trait anxiety demonstrate a relatively blunted sensitivity to threat, as manifested in their slow recognition of the seriousness of cancer symptoms. In the present study we investigated whether the same associations found with rectal cancer patients would generalize to patients with either colon or rectal cancer tumors, since the array of initial symptoms in colon (or colon plus rectal) cancer is much more diverse (e.g., bleeding, change in bowel habits, fatigue, abdominal pain) than in rectal cancer alone (primarily rectal bleeding). Specifically, we hypothesized an interaction between sex and trait anxiety on length of the symptom appraisal interval, such that males who are low in trait anxiety would take significantly longer than high anxiety males to recognize their symptoms were serious.

We also examined the association between symptom appraisal time and the specific location of the primary tumor, which we categorized into either proximal (i.e., primarily ascending or transverse colon) or distal (i.e., primarily descending colon or rectum). This division of sites has been found to provide maximal differentiation between CRC symptom types (i.e., proximal vs. distal symptom “clusters”) (Majumdar et al., 1999). We hypothesized that patients with more distal tumors would take longer to recognize the seriousness of their symptoms as compared to patients with more proximal tumors. This hypothesis is based on the notion that distal tumors are more likely to produce initial symptoms that can easily be misattributed to benign causes (e.g., rectal bleeding attributed to hemorrhoids), thus prolonging symptom appraisal time. Additionally, this hypothesis is supported by the Mitchell et al. (2008) review, which reported some studies showing that longer *total patient interval* was associated with primary tumors in the rectum (vs. the colon) and other studies showing that longer total patient interval was associated with initial symptoms of bleeding or altered bowel habits (vs. abdominal pain). In the present study, we focused more specifically on the duration of the symptom appraisal interval, which is the component of the total patient interval in which tumor location and symptom type are most likely to influence the time it takes for the patient to seek help.

The present study was thus designed to go beyond the Ristvedt & Trinkaus (2008) study by including patients with colon as well as rectal tumors, with the expectation that a broader array of symptom types would provide a strong test of the generalizability of the sex-by-trait anxiety interaction that had previously been found. Relative to the findings reported by Mitchell et al (2008), the present study provided a more focused examination of the roles of tumor location and symptom type, specifically within the more circumscribed context of the symptom appraisal interval.

In addition to trait anxiety and tumor location, we examined associations between symptom appraisal time and age, education, marital status, income, and rural vs. urban residence.

Method

Participants and Procedure

This study was approved by the Institutional Review Board at Washington University School of Medicine (WUSM) in St. Louis, Missouri. Written informed consent was obtained from all participating patients after the nature of the study was fully explained to them. Patients were eligible to participate if they had been diagnosed with a primary colon or rectal tumor within six months prior to recruitment into this study and if they had already undergone colorectal surgery at Barnes-Jewish Hospital at WUSM. All patients who met these criteria were approached for study participation at one of three locations: 1) on the colorectal surgery floor during the post-surgical recovery period, 2) in the colorectal surgery clinic at the time of a follow-up visit, or 3) in the oncology clinic while receiving post-surgical chemotherapy. Patients who agreed to participate but who were unable to finish their questionnaires while in the hospital or during their clinic visit could take the materials home to complete and return by mail.

Self-Report Measures

Patients completed a general study questionnaire that was designed to gather basic demographic data as well as patients' recollections of the onset and course of their cancer-related symptoms and their decision to seek medical help. Derived from previous work (Ristvedt & Trinkaus, 2005; Ristvedt & Trinkaus, 2008), the study questionnaire consisted primarily of items in a checklist or short answer format. Patients also completed a standard psychological measure of trait anxiety.

Demographic information—We documented patients' age, sex, race/ethnicity, level of education, marital status, employment, total household income, and type of health insurance coverage. We geocoded 98 (87.5%) of the 112 residential home addresses and used the Rural Urban Continuum Area (RUCA) indicator of urban/rural status, derived from the U.S. 2000 Census at the census tract level (USDA Economic Research Service, 2005). We categorized patients' census tracts as: (1) small town/rural (population < 10,000); (2) micropolitan (population 10,000–49,999); or (3) metropolitan (population > 50,000).

Initial symptoms and appraisals—Patients were asked to indicate: 1) the type of initial symptom(s) they experienced by selecting from a checklist of 12 of the most common CRC

symptoms (American Cancer Society, 2011), (2) their appraisals of the seriousness of initial symptoms at the time of emergence using a 5-point scale ("not at all" to "extremely"), (3) whether or not they attributed their initial symptoms to cancer at the time of emergence ("yes," "no," or "maybe"), and (4) any alternative attributions for symptoms if they did not initially think they were related to cancer ("hemorrhoids," "diet," "physical injury or stress," "other").

Estimates of time intervals—Patients were asked to estimate the durations of three separate time intervals: symptom appraisal, help-seeking, and diagnostic (Weller et al., 2012). Patients were asked to estimate the duration of the symptom appraisal interval with the following question: *"Think back on the first time you noticed something unusual happening with your body that you now know may have been related to your cancer. How long after your very first symptom did you think that the problem you were having might be serious?"* By asking the question in this way, we were not requiring patients to have known that their bodily changes were symptomatic of any specific disease, but just that they might be signaling the presence of some serious medical condition (Andersen et al., 2009). Patients were asked to estimate the duration of the help-seeking interval by answering this question: *"About how long after you realized your symptoms might be serious did you see a doctor or call for an appointment?"* Together, the symptom appraisal and help-seeking intervals constituted the total patient interval, that is, the time attributable to patients prior to their first contact with a health professional. In order to get an indication of any delays that may have occurred after patients first saw a doctor about their symptoms, we also asked them to estimate the length of time that extended from the first medical contact until the correct diagnosis of CRC was made. Patients estimated the duration of this "diagnostic interval" by answering this question: *"How long after you first saw a doctor was the diagnosis of cancer made?"* Further investigation of contributors to duration of the "diagnostic interval," such as long wait time to get an appointment, was outside the scope of this study. The durations of all time intervals were estimated as continuous variables (i.e., in weeks).

Trait anxiety—Trait anxiety was measured with the Behavioral Inhibition Scale (BIS) of the Behavioral Inhibition / Behavioral Activation Scales (BIS-BAS; Carver & White, 1994). The BIS requires respondents to indicate on a 4-point scale ("very true for me" to "very false for me") how much they agree or disagree with each of 7 items (e.g., *"If I think something unpleasant is going to happen, I usually get pretty 'worked up'"*). Possible scores range from 7 to 28, with higher scores indicating higher levels of trait anxiety. The BIS has demonstrated strong correlations with several other standardized measures of trait anxiety (Carver & White, 1994; Knyazev et al., 2004).

Clinical Data

Information regarding the patients' primary CRC tumors was obtained from Oncology Data Services (ODS), a centralized electronic cancer registry for all patients treated for cancer at Barnes-Jewish Hospital and the Siteman Cancer Center at WUSM. Data in ODS are drawn from internal laboratory, pathology, radiology and operative reports as well as from all outside facilities that may have been involved in the diagnosis and/or treatment of the

patient. Three items of information were gathered from ODS, including site of the primary tumor, stage of the cancer, and tumor grade.

Tumor location—The primary tumor site was classified using the *International Classification of Diseases for Oncology, Third Edition* (ICD-O-3; Fritz et al., 2000) coding system and collapsed into either proximal (comprised of the cecum, ascending colon, hepatic flexure, transverse colon, and splenic flexure) or distal (comprised of the descending colon, sigmoid colon, rectosigmoid junction, and rectum) sites (cf., Majumdar et al., 1999).

Tumor stage—Staging of tumors was accomplished using the TNM scheme (Sobin et al., 2002), which results in stages 1, 2A, 2B, 3A, 3B, 3C, and 4. The subcategories were combined for the present study, resulting in stages 1, 2, 3, and 4.

Tumor grade—Lastly, tumor grade was established according to AJCC guidelines (Greene et al., 2002), resulting in the three categories: poorly differentiated, moderately differentiated, and well-differentiated.

Data Analysis

Initial inspection of the data revealed one extreme outlier in the symptom appraisal time estimates and a small number of missing data points on the psychological measures and in the clinical data. Regarding symptom appraisal time, one female patient reported a symptom duration of 20 years. Although it was highly unlikely that all of her symptoms were due to CRC, given the protracted time frame, it was also impossible to claim that none of her more recent symptoms were due to CRC. Rather than excluding that patient's data from analyses, we truncated her symptom appraisal time to 3 years (156 weeks), which was the next longest time interval that had been reported (by 2 other patients) (cf., Esteva et al., 2007). One patient skipped the BIS scale entirely, and 11 patients missed either 1 or 2 items on one of the psychological measures. Missing items were replaced by the mean of the items that were completed by the patient on that scale. Data missing from ODS included 13 patients without staging information and 2 patients whose tumor sites were listed as "colon, not otherwise specified."

Inspection of the three separate time interval distributions (i.e., symptom appraisal, help-seeking, and diagnostic) revealed that they were all clearly skewed to the right, as is typically found in similar studies (Mitchell et al., 2008), suggesting that most people seek and receive help fairly quickly in response to symptoms. Thus median time interval values were calculated, and nonparametric statistical methods were used. Time-to-event data analytic methods (i.e., Kaplan-Meier, Cox regression) were used to test associations between characteristics of the patients and their tumors and duration of the symptom appraisal time interval. Because not all patients reached the event of interest (i.e., recognition of the seriousness of their symptoms) prior to seeking medical help, time-to-event methods allowed censoring of those cases.

Results

Characteristics of the Sample

A total of 218 patients were approached to participate in this study, although 80 declined for various reasons, including those not able or willing to take the time (n = 42), feeling too ill (n = 20) or not interested (n = 18). Of the remaining 138 patients who were willing to participate, 112 (57 females, 55 males) had begun to experience symptoms that eventually led them to diagnostic evaluation, while the remaining 26 (9 females, 17 males) had their tumors discovered during routine colon cancer screening. Table 1 lists demographic and clinical characteristics of the symptomatic patients.

Time Intervals

Data regarding lengths of the three time intervals (symptom appraisal, help-seeking, and diagnostic) as well as the two summary intervals (patient interval, patient interval + diagnostic interval) are presented in Table 2. Median lengths (in weeks) of each of the time intervals are presented along with counts of the number of patients who fell into each of 4 categories for each of the intervals (i.e., 0–13, 14–26, 27–52, >52 weeks). Most patients (70.5%) determined that their symptoms were serious (i.e., symptom appraisal time) within 13 weeks (i.e., 3 months) after onset. However, close to 20% took greater than 26 weeks (i.e., 6 months), and 8% took more than a year. Once the seriousness of their symptoms was determined, the overwhelming majority of patients (91.9%) sought help within 13 weeks, while only 2 patients took longer than 26 weeks to seek help. The distribution of the diagnostic time interval is the most severely skewed, with all but 6 patients receiving the correct diagnosis within 13 weeks of getting medical attention. Lastly, patients' estimates of the total length of time from symptom onset to CRC diagnosis (i.e., patient interval + diagnostic interval) had a median value of 13.5 weeks. That time was greater than 26 weeks for over one-third of patients and greater than 52 weeks for one-sixth of them.

Correlates of Symptom Appraisal Time

Demographic characteristics—Time-to-event analyses indicated no significant relationships between duration of the symptom appraisal interval and any of the patient demographic characteristics (i.e., age, sex, education, marital status, race, employment status, level of urbanity, total household income, and health insurance status). (See the table in the supplementary online materials for a listing of median symptom appraisal time estimates by demographic subgroup.)

Sex by trait anxiety interaction—A Cox proportional hazards model was used to estimate duration of the symptom appraisal interval by sex of patient and trait anxiety score (BIS score at or below vs. above the median of 19.0). Deviance residuals were used to assess overall model fit, and cumulative martingale residuals were used to assess the proportional hazards assumption for each covariate. BIS scores were strongly associated with symptom appraisal time, although the association was different in male and female patients, as shown in Table 3 (p = 0.007 for the interaction of sex and BIS). Kaplan-Meier models were used to estimate median symptom appraisal times and 95% confidence intervals for each of the 4 subgroups (i.e., male vs. female by low vs. high BIS score). Male patients with low BIS

scores (i.e., low trait anxiety) had significantly longer symptom appraisal times than males with high BIS scores (medians of 17.0 weeks vs. 2.0 weeks), *HR* = 2.1, 95% *CI* [1.1, 4.0]. However, the opposite relationship between BIS score and symptom appraisal time was found among female patients. Female patients with *high* BIS scores had *longer* symptom appraisal times than those with low BIS scores (medians of 26.0 weeks vs. 9.0 weeks), although the difference was not significant, *HR* =0.60, 95% *CI* [0.31, 1.2]. Among all patients with high BIS scores, symptom appraisal times were significantly longer for females than for males (medians of 26.0 weeks vs. 2.0 weeks), HR = 2.8, 95% CI [1.4, 5.6]. But among patients with low BIS scores, symptom appraisal times for male and female patients did not differ significantly (medians of 17.0 weeks vs. 9.0 weeks), HR = 0.78, 95% CI [0.44, 1.4]. It is also interesting to note in Table 3 that there was a higher proportion of censored cases among females (33.9%, or 19 of 56) as compared to males (16.4%, or 9 of 55), indicating that females as a group were twice as likely as males to see a doctor for symptoms they did not yet believe were serious.

Evidence for a sex by trait anxiety interaction in the symptom appraisal process itself is demonstrated by the fact that 9 of the 12 participants who had initially attributed their symptoms to “physical injury or stress” were females, and that 6 of those 9 females had *high* BIS scores. All 3 males who attributed their symptoms to “physical injury or stress” had *low* BIS scores.

Tumor location—A Kaplan-Meier model was used to estimate symptom appraisal time by location of the primary tumor. Compared to patients whose tumors were in a proximal location, patients whose tumors were in a distal location had significantly longer symptom appraisal times, log-rank test statistic = 4.42, $p = 0.036$. Both the nature of patients’ symptoms and their initial attributions regarding the cause of their symptoms were associated with the location of their tumor. As seen in Table 4, abdominal pain was more likely to occur with proximal tumors, while rectal bleeding was more likely to occur with distal tumors. Upon first noticing their symptoms, less than one-third of patients (29.6% of patients with proximal tumors, 30.1% of patients with distal tumors) believed their symptoms were due to cancer. Instead, compared to patients with proximal tumors, patients with distal tumors were initially more likely to attribute their symptoms to hemorrhoids and less likely to attribute them to physical injury or stress.

Discussion

The focus of the present study was on factors associated with the amount of time it takes for an individual to realize that their emerging colorectal cancer symptoms are indeed serious. In line with previous research (Andersen et al., 1995; Cacioppo et al., 1986; Ristvedt & Trinkaus, 2005), we found that – across all participants – the time spent appraising symptoms was the main impediment to receiving expeditious medical attention. Once the determination of seriousness was made, all but a few of the participants sought and received medical attention relatively quickly. In the present study we found that longer symptom appraisal times were associated both with characteristics of the participants and with characteristics of their tumors.

With respect to participant characteristics, the duration of the symptom appraisal interval was significantly associated with an interaction between the sex of the participants and their level of trait anxiety. In a replication of a previous study of patients with rectal cancer (Ristvedt & Trinkaus, 2008), we found that males who were low in trait anxiety took significantly longer to recognize the seriousness of their symptoms as compared to males who were high in trait anxiety (*Mdn* = 17.0 vs. 2.0 weeks). It had previously been suggested that the prolonged symptom appraisal time demonstrated by low anxiety males with rectal cancer could be explained by their relative insensitivity to the threatening nature of their symptoms (Ristvedt & Trinkaus, 2008). This interpretation is corroborated by other studies which indicate that low (vs. high) anxiety males demonstrate a lack of concern regarding physical self-protection in the face of painful (Jones & Zachariae, 2004) and even potentially lethal (Lee & Ristvedt, 2010) situations.

The interactive effect of sex and trait anxiety in the present study was further amplified by the finding that females who were high in trait anxiety had the longest symptom appraisal times (*Mdn* = 26.0 weeks) of any subgroup, far exceeding appraisal times of high trait anxiety *males* (*Mdn* = 2.0 weeks). The reason for long symptom appraisal times among high anxiety females could be that females who have a dispositional tendency toward anxious emotional states are more likely than other groups to misattribute gastrointestinal symptoms to psychological distress, thus not considering that their colorectal cancer symptoms could be due to a potentially lethal condition. In support of this interpretation, and as noted earlier, we found that 6 of 12 participants who had initially attributed their emerging symptoms to “physical injury or stress” were females who were high in trait anxiety, whereas the other 6 participants (3 females and 3 males) were all low in trait anxiety. This interpretation is also consistent with the “stress-illness rule,” which has been used within the CSM theoretical framework to describe the cognitive mechanism through which some individuals under certain circumstances are prone to wrongly attribute their illness symptoms to emotional distress (Baumann et al., 1989; Cameron, 2003; Leventhal et al., 2003). Why this phenomenon might be more likely to occur among females as compared to males in our study is not clear. However, there is ample evidence showing that females are approximately twice as likely as males to suffer from functional gastrointestinal disorders and symptoms (Cain et al., 2009; Mayer et al., 1999; Pickett-Blakely et al., 2010), which may explain why females would be more likely to form the mistaken conclusion that gastrointestinal symptoms are a manifestation of a benign, stress-related condition. This interpretation of our data, although intriguing, is only preliminary. Research is clearly needed to further investigate the interrelationships among sex, trait anxiety, and symptom appraisal processes in CRC.

Regarding tumor characteristics, patients with distal tumors had significantly longer symptom appraisal times than patients with proximal tumors. This finding may be explained by the fact that distal tumors were also more likely to produce rectal bleeding as an initial symptom and more likely to be misattributed to hemorrhoids as a benign cause. Although these data are consistent with the findings by Mitchell et al (2008), our specific focus on the symptom appraisal interval (vs. the total patient interval) offers a clearer indication of the

links between tumor location, symptom type, patients' attributions, and symptom appraisal time.

There are two notable limitations to this study. First, because investigations of responses to developing cancer symptoms are retrospective, researchers must rely on participants' reporting of events that may have occurred up to many months in the past. However, confidence in the findings of such investigations can be built by carefully constructing study questions and by relating the results to those from similar studies, both of which we have tried to do here. The second limitation has to do with the fact that we investigated associations between individuals' appraisals of *past* symptoms and *current* dispositional characteristics. However, research has documented that the BIS demonstrates: (a) significant temporal stability over the course of 2–3 years (Takahashi et al., 2007), (b) moderate influence by heritable factors (Takahashi et al., 2007), and (c) significant associations with individual variation in the serotonin transporter (5-HTTLPR) genetic polymorphism (Whisman et al., 2011). Together, these findings lend confidence to the supposition that BIS scores measured at the time of study participation were reflective of BIS scores that may have been measured when CRC symptoms were emerging.

The present study highlights the critical importance of the symptom appraisal process in the early detection of CRC. In addition, this study makes a unique contribution to the literature by simultaneously investigating disparate characteristics – of both the patients (i.e., trait anxiety, sex) and their tumors (distal vs. proximal location) – that can impact symptom appraisal duration and that could ultimately impede the pursuit of medical help. The role of trait anxiety, particularly in combination with patient sex, had not previously been studied in the context of symptom appraisal in CRC. In addition, although tumor location has previously been implicated in the duration of total "patient delay" (Mitchell et al., 2008), the present study offers greater clarification regarding the mechanism through which tumor location influences the symptom appraisal process. From a theoretical standpoint, results from the present study lend support to the CSM framework, which holds that the development of an illness representation may be influenced by concrete experience (somatic symptoms), abstract concepts (illness labels), and anxiety (Cameron, 2003; Leventhal et al., 2011).

From a practical standpoint, findings from this study could be used to refine efforts to educate the public about the nature of CRC symptoms and the importance of early recognition. Unfortunately, public awareness of CRC symptoms is still generally low (McCaffery et al., 2003; Robb et al., 2009). Large-scale efforts to promote awareness – such as the Bowel Cancer Australia initiative – have had negligible, if any, impact on medical consultation rates for CRC symptoms (Courtney et al., 2012). In that regard, the data presented here offer some insights into ways in which educational efforts might be made more effective. For instance, understanding the dispositional characteristics of people who take the longest amount of time to recognize the seriousness of their symptoms could assist in knowing whom to specifically target with educational messages as well as what those messages should say. The person who might be inclined to neglect their symptoms out of a more general tendency to dismiss potential hazards may need to be educated about the life-threatening ramifications of ignoring certain types of bodily changes. On the other hand, the

person who might be prone to endure their symptoms out of a mistaken belief that they are simply a physical manifestation of a fretful temperament may need to be educated about what psychological stress can and cannot do. In a similar way, understanding the types of CRC symptoms that are least likely to raise concern could assist in knowing the kind of information to emphasize in patient and public education. People need to know, for example, that even though rectal bleeding is indeed commonly caused by hemorrhoids, it is also the GI symptom that is most strongly associated with cancer (Astin et al., 2011) and therefore one that should definitely prompt medical investigation (Adelstein et al., 2011). The present research identifies symptom misattributions that could be targeted in future interventions as well as the psychological characteristics of individuals who are most likely to make those misattributions.

Lastly, the findings from this study should encourage clinicians to maintain an objective approach toward their patients' reports of GI symptoms and not to be swayed by inclinations to explain them away. Failure to initiate endoscopic evaluation in response to symptoms suggestive of CRC happens much too often (Singh et al., 2009), which may be one reason that missed diagnosis of CRC is one of the most common causes for ambulatory malpractice claims (Gandhi et al., 2006; Phillips et al., 2004). In summary, knowing more about the factors that influence the CRC symptom appraisal process could ultimately shorten the time to diagnosis and mitigate undue damage to both patients and their doctors.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Demographic and Clinical Characteristics of Study Participants (n=112)

Age at interview, mean years ± S.D. (range)	59.3 ± 13.4 (27 – 87)
Sex, *n* (%)	
Female	57 (50.9)
Male	55 (49.1)
Education, *n* (%)	
Less than high school	13 (11.6)
High school graduate/GED	39 (34.8)
Some college	29 (25.9)
College graduate or more	30 (26.8)
Missing	1 (0.7)
Marital Status, *n* (%)	
Married	67 (59.8)
Widow(er)	19 (17.0)
Single	15 (13.4)
Separated/divorced	11 (9.8)
Race, *n* (%)	
Non-Hispanic White	91 (81.2)
Non-Hispanic African-American	15 (13.4)
Other	4 (3.6)
Missing	2 (1.8)
Employment, *n* (%)	
Full time	42 (37.5)
Part time	12 (10.7)
Retired	35 (31.3)
Other (i.e. disabled, homemaker, unemployed, medical leave)	23 (20.5)
Level of Urbanity, *n* (%)	
Metropolitan	68 (60.7)
Micropolitan	10 (8.9)
Small town and rural	20 (17.8)
Missing	14 (12.5)
Total household income, *n* (%)	
≤ $19,999	28 (25.0)
$20,000 to $34,999	16 (14.3)
$35,000 to $49,999	22 (19.6)
$50,000 to $74,999	16 (14.3)
≥ $75,000	25 (22.3)
Missing	5 (4.5)
Health insurance status, *n* (%)	
Managed care (HMO, PPO)	53 (47.3)
Medicare	39 (34.9)

Other (i.e., Medicaid, VA)	14 (12.5)
Not insured	6 (5.4)
Tumor location, *n* (%)	
Proximal	27 (24.1)
Distal	83 (74.1)
Colon NOS	2 (1.8)
Tumor grade/differentiation, *n* (%)	
Poorly differentiated	27 (24.1)
Moderately differentiated	73 (65.2)
Well differentiated	6 (5.4)
Not determined or N/A	6 (5.4)
TNM Stage, *n* (%)	
I	21 (18.8)
II	22 (19.6)
III	34 (30.4)
IV	22 (19.6)
Missing	13 (11.6)

Note: Proximal colon = cecum, ascending colon, hepatic flexure, transverse colon, and splenic flexure; Distal colon = descending colon, sigmoid colon, rectosigmoid junction, and rectum.

Table 2

Estimated Lengths of Time Intervals

Time Interval	Patients per group *n* (%)
Symptom appraisal interval (*Mdn* = 8.0 weeks) (*n* = 112)	
0 – 13 weeks	79 (70.5)
14 – 26 weeks	12 (10.7)
27 – 52 weeks	12 (10.7)
> 52 weeks	9 (8.0)
Help-seeking interval (*Mdn* = 1.0 weeks) (*n* = 111)[a]	
0 – 13 weeks	102 (91.9)
14 – 26 weeks	7 (6.3)
27 – 52 weeks	1 (0.9)
> 52 weeks	1 (0.9)
Patient interval[b] (*Mdn* = 10.0 weeks) (*n* = 111)	
0 – 13 weeks	61 (55.0)
14 – 26 weeks	17 (15.3)
27 – 52 weeks	17 (15.3)
> 52 weeks	16 (14.4)
Diagnostic interval (*Mdn* = 2.0 weeks) (*n* = 111)[c]	
0 – 13 weeks	105 (94.6)
14 – 26 weeks	4 (3.6)
27 – 52 weeks	2 (1.8)
> 52 weeks	0 (0.0)
Patient interval + diagnostic interval (*Mdn* = 13.5 weeks) (*n* = 110)	
0 – 13 weeks	55 (50.0)
14 – 26 weeks	15 (13.6)
27 – 52 weeks	22 (20.0)
> 52 weeks	18 (16.4)

Note.

[a] One patient did not provide an estimate of the duration of the help-seeking interval.

[b] Patient interval = symptom appraisal + help-seeking.

[c] One patient did not provide an estimate of the duration of the diagnostic time interval.

Table 3

Duration of Symptom Appraisal Interval by Sex and Trait Anxiety (BIS) Score (n = 111)[a]

Subgroup	*n*	Censored *n* (%)	Median Appraisal Time weeks (95% C.I.)[b]
Females			
Low BIS	29	9 (31.0)	9.0 (4.0 – 13.0)
High BIS	27	10 (37.0)	26.0 (8.0 – 61.0)
Males			
Low BIS	39	8 (20.5)	17.0 (9.0 – 26.0)
High BIS	16	1 (6.2)	2.0 (1.0 – 9.0)

Note. p = 0.007 for the interaction of sex and trait anxiety (BIS) score.

[a] One patient did not complete the BIS scale.

[b] Medians and 95% confidence intervals were estimated by a Kaplan-Meier model.

Table 4

Initial Symptoms and Patients' Attributions by Tumor Site (n = 110)[a]

	Tumor Site			
Variable	**Proximal *n* = 27**	**Distal *n* = 83**	**χ^2 (1)**	***p***
Initial symptom, *n* (%)[b]				
Bleeding	7 (25.9)	57 (68.7)	15.30	.001
Change in bowel habits[c]	13 (48.1)	43 (51.8)	0.11	.741
Malaise[d]	11 (40.7)	19 (22.9)	3.27	.070
Weight loss (unintentional)	5 (18.5)	13 (15.7)	0.12	.728
Abdominal pain	8 (29.6)	9 (10.8)	5.50	.019
Rectal pain/pressure	3 (11.1)	9 (10.8)	0.00	.969
Alternative attributions, *n* (%)				
Hemorrhoids	3 (11.1)	33 (39.8)	7.59	.006
Diet	2 (7.4)	13 (15.7)	1.18	.278
Physical injury or stress	6 (22.2)	6 (7.2)	4.71	.030

Note:

[a] Specific tumor site was not available on two patients, whose sites were listed in the Oncology Data Services (ODS) electronic registry as "colon, not otherwise specified";

[b] Several patients reported multiple initial symptoms;

[c] Change in bowel habits combines constipation, diarrhea, altered stools (e.g., narrow, dark, containing mucous).

[d] Malaise combines loss of appetite, nausea, fatigue, feeling ill.