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Sex differences in responding to rectal cancer symptoms

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Abstract

Many people who develop cancer symptoms wait inordinate amounts of time before seeking medical attention. Studies have found that symptom appraisal time - the time that passes before the individual concludes that their symptoms could be serious - accounts for most of the total delay time across subjects. It is thus important to understand the individual characteristics associated with slow recognition of dangerous symptoms. In this study, 62 patients (38 males) recently diagnosed with rectal cancer answered questions regarding the development of symptoms as well as their decisions and behaviors prior to seeking help. One subgroup of patients - males with the lowest scores on a measure of trait anxiety - took significantly longer to recognize the seriousness of their symptoms as compared to all other patients. This finding is discussed in the context of recent studies where the interaction of sex and negative affect is related to symptom reporting and other health-related behaviors.

Keywords

Harm avoidance; patient delay; rectal cancer; sex differences; symptom appraisal; trait anxiety

Introduction

It is estimated that 41,930 Americans will have been diagnosed with rectal cancer in 2006, equally split between males (56.2%) and females (American Cancer Society, 2006). While the 5-year survival rate is around 60%, survival chances can be increased by the fact that rectal cancer is easily detected in its earliest stages, either through routine screening (i.e., digital rectal examination, endoscopy) or through the emergence of fairly salient first symptoms (i.e., rectal bleeding, in most cases). However, a large number of people who develop symptoms of rectal cancer wait an inordinate amount of time before seeking help (Ristvedt & Trinkaus, 2005). As in other cancers in which the problem of patient delay has been studied, most of the time between symptom onset and medical consultation (about two-thirds) is initially spent with the patient believing that their symptoms are due to some benign disease (i.e., symptom appraisal time). Most people act fairly quickly once they realize that their problem could be serious, although a smaller number will then hesitate out of fear and avoidance (Andersen, Cacioppo, & Roberts, 1995). Due to the significant role of the symptom appraisal process in help-seeking, it is important to understand the characteristics of those individuals who are slower to recognize the dangerousness of their symptoms.

Two consistent correlates of symptom reporting and health behavior, aside from objective medical events or conditions, are sex and negative affect. With regard to sex differences, males are seen as generally neglectful of their health and reluctant to seek professional help for symptoms (Addis & Mahalik, 2003). For example, men are more likely than women to have never contacted a doctor, and almost twice as likely to be without a usual place of health care (Lethbridge-Cejku & Rose, 2006). On the other hand, most studies have shown that females report more frequent and more intense symptoms than males, even when gynecologic symptoms are excluded (Barsky, Peekna, & Borus, 2001; Gijsbers van Wijk & Kolk, 1997). Several explanations for this difference have been offered, including differences in: somatic perception, symptom labeling and reporting, socialization regarding the expression of distress, and incidence of mood and anxiety disorders (Barsky et al., 2001). However, no conclusions have been reached.

One might hypothesize, then, that males would take longer than females to respond appropriately to serious symptoms. However, the findings regarding sex differences in studies of delayed help-seeking have been equivocal. While one study has found that males were more likely to delay seeking help for colon and rectal cancers (Young, Sweeney, & Hunter, 2000), results from other studies have been mixed or have showed no difference (Gonzalez-Hermoso, Perez-Palma, Marchena-Gomez, Lorenzo-Rocha, & Medina-Arana, 2004; Marshall & Funch, 1986; Robinson, Mohilever, Zidan, & Sapir, 1986). In addition, no differences have been found in most studies of other cancers that afflict both sexes about equally (Neal & Allgar, 2005).

The other consistent correlate of symptom reporting and health behavior is negative affect. Higher levels of negative affect, manifested in the degree of anxiety, depression, and other negative emotions (Cloninger, 1987; Costa & McCrae, 1992; Watson & Clark, 1984), are associated with greater frequency of somatic complaints (Watson & Pennebaker, 1989) as well as over-reporting of symptoms after controlling for physiological markers of disease (Feldman, Cohen, Doyle, Skoner, & Gwaltney, 1999; Williams et al., 2002). Several explanations for these findings have been offered, but the one that receives the most empirical support comes from Watson and Pennebaker (1989), who posited that the correlations between negative affect and symptom reporting “reflect a common, underlying disposition of somatopsychic distress” (p. 235). Their “symptom perception hypothesis” states that subjects who are high in negative affect are also more likely to notice and complain about any negative changes in physical functioning. If those people who are more prone to negative affect are quicker to construe ambiguous symptoms as serious, then we might hypothesize that those who are disinclined to negative affect would be slower to respond to ambiguous symptoms, even when those symptoms turn out to be serious.

It has long been suggested that low levels of anxiety are associated with longer delay times (Antonovsky & Hartman, 1974), although there have been few studies that have tested this hypothesis. However, we recently conducted a study in which one segment of total delay time - symptom appraisal time - was associated with low scores on a measure of trait anxiety (Ristvedt & Trinkaus, 2005). That measure was the Harm Avoidance scale of the Temperament and Character Inventory (TCI-HA), which is a seven-dimension measure of personality derived from Cloninger’s biopsychosocial model (Cloninger, Przybeck, Svrakic, & Wetzel, 1994). The TCI-HA correlates highly with other personality measures designed to reflect the same construct of negative affectivity, including the Neuroticism scales of the EPQ (Eysenck & Eysenck, 1976) and the NEO-PI (Costa & McCrae, 1992), and the BIS scale of the BIS/BAS (Carver & White, 1994). However, the items on the TCI-HA tend to focus on anxiety and worry.

That study thus provided evidence that patients with low levels of trait anxiety take longer than others to recognize the seriousness of their symptoms (Ristvedt & Trinkaus, 2005). But

contrary to expectation, there was no difference between males and females in symptom appraisal time. In our previous analysis, however, we looked only at the first-order effects of demographic and psychological variables considered together in a multivariate analysis; no interactions were included because none were hypothesized at that time. Several recent reports have advocated the consideration of both sex and negative affect together in studies of symptom reporting and health-related behaviors (Gijsbers van Wijk & Kolk, 1997). In one study, sex had a moderating effect on the relationship between neuroticism and retrospective symptom-reporting, such that the path between neuroticism and symptom reports was partially mediated by self-focused attention for females but not for males (Williams & Wiebe, 2000). Another study found a significant correlation between trait negative affect and symptom severity ratings in retrospective reports for females but not for males (Van Diest et al., 2005). In addition, several studies have found a clear relationship between sex and negative affect, where females tend to report greater negative affect than males (Lynn & Martin, 1997), including a study of 804 community subjects (Cloninger, Bayon, & Przybeck, 1997) in which females had significantly higher scores on the TCI-HA scale (T. Przybeck, personal communication).

The present article is a report of a secondary analysis of our data, with specific attention to the role of sex, Harm Avoidance measure, and the interaction between the two, in their associations with symptom appraisal time. Specifically, we wanted to test whether male patients who were low in trait anxiety would report longer symptom appraisal times as compared to the other patients.

Methods

Participants and procedure

Participants were patients who had been recently diagnosed with primary rectal tumors and who had been treated in the Section of Colon and Rectal Surgery at the Washington University School of Medicine. A full description of the procedure and materials can be found in the original study (Ristvedt & Trinkaus, 2005). Data were collected on 62 subjects for these analyses. Twenty-four of the subjects were female and 38 were male. Fifty-nine of the subjects were Caucasian and three were African-American. The age at diagnosis ranged from 33 to 83 years, with a mean of 59.9 ($SD = 12.4$). Level of education ranged from 1st grade to postgraduate work.

Materials

Patients were given materials to complete at home and return by mail. The two principal instruments were: (1) the Study Questionnaire, which was designed by the first author to collect information about history of symptoms, perceptions of those symptoms, and pertinent decision-making and behaviors during the time period prior to medical consultation, and (2) the Temperament and Character Inventory (TCI; Cloninger et al., 1994).

The Study Questionnaire—The Study Questionnaire was made up of several questions about the recognition of seriousness of symptoms, the decision to seek medical help, and the actual pursuit of medical help. Only two questions were of particular interest in the present analysis. Subjects were asked to think back on the time when they first realized that their symptoms might be serious, and symptom appraisal time was estimated by asking, “How long after your very first symptom did this occur?” Total delay time was estimated by asking, “About how long was it after your very first symptom that you first saw a doctor about it?” The mean symptom appraisal time was 17.5 weeks ($SD = 24.1$; range = 1-104), while the mean total length of time prior to medical consultation was 25.5 weeks ($SD = 40.6$; range = 2-260), so that symptom appraisal time accounted for approximately 68.7% of the total time.

The Temperament and Character Inventory—Subjects completed the short form of the TCI. The 20-item TCI-HA has demonstrated a coefficient alpha ranging from 0.78 to 0.85 and test-retest correlations ranging from 0.73 to 0.84 over an average of 2.1 years (Heath, Cloninger, & Martin, 1994). The mean of TCI-HA scores across all subjects in the present study was 6.67 (SD = 4.46; range = 1-18), which is comparable but a little lower than the mean calculated from a community sample of 300 subjects (Mean = 7.6, SD = 4.5; Cloninger et al., 1994). Coefficient alpha for this study was 0.83.

Statistical analyses

A Cox proportional hazards time-to-event analysis was conducted for three reasons (Kleinbaum, 1996). First, it is the method of choice with measures of event occurrence, which tend to be nonnormally distributed. The time period of interest began with the onset of symptoms and ended at the point when subjects recognized the seriousness of their symptoms (i.e., symptom appraisal time). Second, time-to-event analysis allows data from subjects who do not reach the event of interest to contribute to the analysis through censoring. In this study, we were able to include data from subjects who did not suspect that their symptoms were serious prior to seeking medical consultation. Third, Cox regression analysis allows estimation of covariate effects. We wanted to test whether the length of symptom appraisal time was associated with TCI-HA scores, sex, or an interaction between the two. Based on previous work, TCI-HA scores were divided into tertiles - low, medium, and high (Ristvedt & Trinkaus, 2005). There was no evidence of underlying differences between male and female participants in education, race, or age at diagnosis, so none of these were included as covariates.

Results

Relationships between sex, TCI-HA, and symptom appraisal time

Females in the present study had TCI-HA scores ranging from 1 to 18, while males had scores ranging from 1 to 14. Results of Mann-Whitney tests showed that females had significantly higher scores than males (8.71 vs. 5.37; $z = 2.653$, two-tailed $p = 0.008$). Cox regression analyses showed no sex differences in symptom appraisal times (Chi-square = 0.45, n.s.). Table I shows the descriptive statistics for both TCI-HA score and symptom appraisal time corresponding to each of the six patient groups in the sex by TCI-HA interaction. As can be seen in the first column of Table I, the distribution of TCI-HA scores is different for males *versus* females, with a greater number of females in the high TCI-HA tertile ($n = 13$) as compared to females in the middle ($n = 7$) and low ($n = 4$) tertiles. For males, the smallest number was in the high TCI-HA tertile ($n = 6$), as compared to males in the middle ($n = 17$) and low ($n = 15$) tertiles. This difference in distributions of TCI-HA score by sex is reflective of the sex difference in mean TCI-HA scores reported above. It should be noted that TCI-HA tertiles were calculated on the entire group of subjects, rather than separately for males and females, in order to document the sex-related difference in frequency distributions of scores. It can be seen in the second column that the TCI-HA means for each of the three tertiles are comparable for females *versus* males (2.00 vs. 2.00; 5.57 vs. 6.18; 12.36 vs. 11.50). The last three columns of Table I show the mean, median, and range of the symptom appraisal times for each of the six groups. The largest mean, by a substantial margin, was for the 15 males who had the lowest TCI-HA scores (i.e., 33.60 weeks). The next highest mean was for the 7 females who fell into the middle tertile of TCI-HA scores (i.e., 17.86), while the other 4 means were in the same general range.

We then conducted the Cox proportional hazard analysis of symptom appraisal time, with the covariates being sex, TCI-HA, and the sex by TCI-HA interaction. Thirteen of the 62 subjects (21.0%) were censored because they sought medical attention for their symptoms before suspecting that they were serious. The global null hypothesis was rejected (Chi-Square = 9.97,

$df = 3, p = 0.019$), indicating that some combination of the three covariates was associated with length of symptom appraisal time. Neither sex nor TCI-HA score were independent predictors in this model, while the interaction between the two did reach statistical significance ($p = 0.036$). The hazard ratio for the interaction was 0.19, with a range from 0.09 to 0.90, indicating that males with low TCI-HA scores were at least 10% less likely to recognize the seriousness of their symptoms at any one point in time, as compared to all other participants. Figure 1 shows Kaplan-Meier survival curves of symptom appraisal time for each of the six subgroups; each downturn in a line represents another person (or group of persons) reaching the event of interest. This presentation makes it clear that the males who had the lowest scores on the TCI-HA scale took significantly longer than the other patients to recognize the seriousness of their symptoms.

Discussion

Many studies have found two consistent correlates of higher rates of reporting physical symptoms: female sex and high levels of negative affect. However, little research has been done on individual characteristics associated with a *blunted* response to symptoms that turn out to be serious. In a previous study, we found that low Harm Avoidance was associated with longer symptom appraisal times, but there was no effect of sex (Ristvedt & Trinkaus, 2005). In the present analysis, however, we took a closer look by examining the interaction between sex and Harm Avoidance in the prediction of symptom appraisal time. Here, a subset of males who were low in Harm Avoidance took longer than all the others to realize that their symptoms were serious.

Several studies have shown a similar interaction between sex and anxiety in their effect on self-protective behaviors. Specifically, males with low levels of anxiety seem to differ from others in their relative lack of concern regarding threatening situations and in a slower response to potential bodily harm. In a longitudinal study of 4070 individuals, low anxiety assessed at age 13 was associated with a significantly higher probability of death by accident by the age of 25 compared to those with higher anxiety levels (Lee, Wadsworth, & Hotopf, 2006). Pertinent to the present study, a follow-up analysis of the data showed that the subgroup most likely to die by accident were low anxiety males as compared to high anxiety males, low anxiety females, and high anxiety females (W. E. Lee, personal communication). In addition, a number of studies report a significant correlation between anxiety level and pain ratings in males but not in females. In two studies involving the cold pressor test, low anxiety males demonstrated higher pain tolerance than high anxiety males, who did not differ from either low anxiety or high anxiety females (Jones & Zachariae, 2004; Jones, Zachariae, & Arendt-Nielsen, 2003). The findings that low anxiety males were uniquely unresponsive to direct threats to physical well-being bears a similarity to the present report.

At this point, it would be difficult to integrate these disparate findings into a cohesive understanding of sex differences in delayed or muted responses to serious physical threats. For one thing, there are weaknesses in the present study that need to be taken into account. First, Table I shows that there was a wide range of symptom appraisal times among males with low TCI-HA scores (1-104 weeks), suggesting that there were some males with low TCI-HA scores who did quickly recognize the seriousness of their symptoms. Whatever differentiates them from the slower males remains unknown. Second, as in all studies of delayed treatment for symptoms, there was heavy reliance on subjects' retrospective reports. However, the initial symptoms of rectal cancer almost always include rectal bleeding, which should provide a memorable onset to the problem when patients are asked to recount the onset and course of their symptoms. Finally, the original study was not designed to identify interactions between predictors of symptom appraisal time, so the present finding needs to be verified by an independent study.

Still, all of these studies taken together do suggest that males and females tend to respond in different ways to threats to well-being. One possible explanation is that males tend to be lower in negative affect, and that negative affect is the only mediator of response to symptoms. In this study, females had higher TCI-HA scores than males, which is in keeping with other studies that show that females tend to report greater negative affect than males (Lynn & Martin, 1997). However, there is also evidence to suggest that females report more frequent and intense symptoms than males even after controlling for negative affect (Kroenke & Spitzer, 1998).

Alternatively, it has been suggested that any differences between males and females in their response to symptoms might be found in the qualitative nature of that response rather than in the total time that it takes to reach the same ultimate resolution (Marshall, Gregorio, & Walsh, 1982). Differences between males and females could be due in part to the way in which negative affect informs their decision-making. In the present study, a subset of males seem to be relying on a “complacent” affect heuristic (Slovic, Finucane, Peters, & MacGregor, 2002) by telling themselves “I’m not worried, so I must be fine”. With regard to health in particular, males tend to worry less and have lower perceptions of risk while females tend to be more cautious (Peters, Slovic, Hibbard, & Tusler, 2006). Taken to extremes, both of these tendencies could translate into delayed help-seeking, albeit in very different forms, should symptoms emerge. This possibility needs to be examined in future research.

Given the number of people who still delay seeking help and the dire consequences that often follow, it is important to understand the individual characteristics that could put one at risk. By studying the role of sex and negative affect together in the response to bodily changes, it might be possible to gain a clearer understanding of the perceptions, decisions, and behaviors that influence the utilization of health care. The present analysis suggests that it might be an overgeneralization to say that males wait longer than females to seek help for serious symptoms. Rather, it might be more accurate to say that one particular subset of males tends to take longer to appreciate the seriousness of their symptoms, which can then result in delayed help-seeking. Future work should be done to see if this finding holds true and to develop a full description and understanding of this group. Public health efforts could then target such at-risk individuals and learn how to communicate with them in more effective ways.

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Symptom Appraisal by Sex and TCI–HA Tertile

Figure 1.
Symptom appraisal time by sex and TCI-HA tertile.

Table I
TCI-HA Score and symptom appraisal time by sex and TCI-HA tertile

Variable	n	TCI-HA score Mean (SD)	Symptom appraisal time (weeks)		
			Mean (SD)	Median	Range
Females					
TCI-HA tertile					
Low	4	2.00 (0.82)	10.25 (8.62)	9.0	3-20
Middle	7	5.57 (1.27)	17.86 (17.17)	15.0	1-52
High	13	12.46 (3.28)	14.23 (15.75)	12.0	1-52
Males					
TCI-HA tertile					
Low	15	2.00 (0.93)	33.60 (37.90)	13.0	1-104
Middle	17	6.18 (1.47)	10.24 (16.22)	3.0	1-65
High	6	11.50 (2.07)	9.83 (12.58)	2.5	1-26