

## ALIMENTARY TRACT

## Gender Differences in Manning Criteria in the Irritable Bowel Syndrome

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The objective of this study was to determine if gender differences exist when using the Manning criteria for diagnosis of irritable bowel syndrome. In an outpatient setting, 61 women and 36 men with entry complaints of abdominal pain, altered bowel habits, or both underwent full evaluation by board-certified/eligible gastroenterologists who also systematically rated the presence or absence of the six Manning criteria. Irritable bowel syndrome was defined as the absence of an organic disease explanation for the entry complaints. This determination was made by two other board-certified gastroenterologists after patients had been in the study for 9 months. These raters were independent of the study and rated the transcripts of patients' clinic visits, all other available clinical data from this and other clinics, all laboratory data obtained during the 9-month study period, and the results of a 9-month telephone follow-up to patients and their physicians. Sixty-five percent of the study population had no organic disease explanation for the entry symptoms, thereby representing irritable bowel syndrome for this study. A similar proportion and type of organic disease and irritable bowel syndrome were experienced by men and women. For the total sample of 97 subjects, the correlation of the Manning criteria with irritable bowel syndrome was 0.22 ( $P < 0.01$ ). In the 61 women, correlation between the Manning criteria and irritable bowel syndrome was significant ( $r = 0.47$ ;  $P < 0.01$ ). In the 36 men, however, the correlation was in the opposite direction, although it was not significant ( $r = -0.16$ ). It was concluded that significant gender differences exist when using the Manning criteria for the diagnosis of irritable bowel syndrome and that the Manning criteria were not of diagnostic value in men.

Irritable bowel syndrome (IBS) is characterized by abdominal pain, alteration of bowel habits, or both as the primary complaints (1-3). In spite of extensive study, no organic disease basis has been identified, and there is no agreement regarding its pathophysiological mechanism (4). Irritable bowel syndrome is expensive as well as common (5,6) and has an estimated prevalence between 14% and 22% in selected nonpatient populations (7,8). There is, however, no definitive diagnostic approach (1-4) and no gold standard diagnosis (9). Rather, physicians have relied on multiple laboratory testing and other diagnostic investigations to exclude an organic disease basis for the symptoms (1-4).

Important attempts have been made to make a positive diagnosis of IBS from physical symptoms. The questionnaire study of Manning et al. (2) (of a population presenting with abdominal pain, altered bowel habits, or both) showed that the more of the following symptoms were reported, the more likely was the diagnosis of IBS: abdominal distension, relief of pain with bowel movement, loose and more frequent stools with the onset of pain, the presence of mucus in the stool, and an incomplete sense of evacuation. In a similar study, Kruis et al. (3) administered a questionnaire concerning many of these symptoms to a comparable study population. They found that the following symptoms, when combined, correlated highly with IBS: abdominal pain, flatulence, and irregular bowel habits. They also recommended that simple criteria concerning organic disease be used in conjunction with them. Unfortunately, the most inclusive use of both sets of criteria is associated with a

high false-positive rate; i.e., the erroneous diagnosis of IBS when organic disease is present (2,3). Nonetheless, these are the best available diagnostic criteria (2,3).

Gender effects on a diagnosis of IBS were not evaluated by Manning et al. (2) or Kruis et al. (3). Nevertheless, it has been proposed that gender differences exist in many medical disorders, both inside (9,10) and outside gastroenterology (11,12), although they are not invariably noted (13,14). This article reports an unexpected finding concerning gender and the Manning criteria. It was detected from the data collected during a previously reported study demonstrating the lack of diagnostic value of psychosocial factors for IBS (15). As part of this prospective study, we used the Manning criteria, in addition to psychosocial variables, as predictors of IBS. Although the Manning criteria were associated with IBS, further analysis by gender showed that they were not associated with IBS in men. This paper details these findings.

## Materials and Methods

### Subjects

This study was approved by two appropriate institutional review boards. Of 279 new patients presenting consecutively to the gastroenterology clinic, 148 met entry criteria, similar to those of Manning et al. (2) and Kruis et al. (3), for this study: at least 1 month of continuous or intermittent abdominal distress, altered bowel habits, or both. Of the 148 candidates, 17 refused to participate (emotional distress, lack of time or interest, or no reason given) and another 34 had incomplete data sets (failure to return for follow-up). Of the remaining 97 subjects making up the study sample, 61 were women and 36 were men; 84% were white and 64% were married. The mean age was 49 years for men and 46 years for women. Of the patients with incomplete data sets, there were 23 women and 11 men.

### Dependent Measure

Irritable bowel syndrome was operationally defined as the absence of an organic disease explanation for the entry complaints, as in the studies of Manning et al. (2) and Kruis et al. (3). Irritable bowel syndrome was represented by the averaged rating of two board-certified gastroenterologists who were independent of the study and unaware of its design or intent. The raters reviewed typed copies of the patients' study visit charts, all available medical information from before the study, all laboratory studies and other investigative procedures during the 9 months of the study, and the results of a 9-month telephone follow-up. Each rated all 97 patients following a 3-hour period of instruction and practice. When both IBS and organic disease were present, raters were instructed to make the diagnosis that best explained the entry complaints. Because ratings were on an interval scale, agreement between raters was calcu-

lated using a zero-order correlation coefficient. Interrater reliability, shown by a Pearson correlation, was .75. Ratings ranged from 1 (indicating a confident diagnosis of organic disease) to 6 (indicating a confident diagnosis of nonorganic disease), with a mean for the entire group of 3.69 and a standard deviation of 1.39. Of the 61 women, the mean score was 3.63 (SD, 1.41). Of the 36 men, it was 3.78 (SD, 1.36), which was not significantly different.

Dichotomizing the study group's ratings at 3.5 and comparison of raters showed that the raters disagreed on 12 of the 97 cases. Where raters agreed, 30 cases were diagnosed as having organic disease and 55 as IBS. For testing the diagnostic value of the Manning criteria, all 97 cases were used to represent the dependent variable. The organic diseases were not different in men and women, as determined by a review of clinical records, and represented a typical outpatient population with the majority exhibiting peptic ulcer disease, inflammatory bowel disease, symptomatic gall stones, or infectious diarrhea.

### Independent Measure

The Manning criteria (2) were represented by the six symptoms already noted (Table 1) and were elicited directly from patients by three board-certified/eligible, university-based gastroenterologists practicing in the two clinics where the study was conducted. The six Manning criteria were averaged to form one score. Using a range of 1 to represent the absence of each item and 2 to represent its presence, the mean score for the total sample was 1.25 (SD, 0.26). Internal consistency, using Cronbach's  $\alpha$ , was 0.65. The mean scores for men and women were 1.21 (SD, 0.27) and 1.28 (SD, 0.26), respectively, and they did not differ significantly. For the dropout group, the mean score was 1.63 (SD, 0.23), which is significantly higher ( $P < 0.01$ ) than the study

Table 1. Manning Criteria Item Analysis by Gender

Men (n = 36)		Women (n = 61)		Manning criteria
Yes (%) <sup>a</sup>	r <sup>b</sup>	Yes (%) <sup>a</sup>	r	
22.2	-0.35 <sup>c</sup>	18.0	0.28 <sup>c</sup>	Onset of pain associated with more frequent bowel movements than normal
27.8	-0.22	23.0	0.35 <sup>d</sup>	Onset of pain associated with looser bowel movements than normal
22.8	-0.03	32.2	0.17	Pain is relieved by bowel movements
13.9	0.06	42.6 <sup>e</sup>	0.04	Visible abdominal bloating is present
25.0	0.26	31.1	0.42 <sup>e</sup>	> 1/4 bowel movements associated with sense of incomplete emptying
13.9	-0.38 <sup>e</sup>	19.7	0.29	> 1/4 bowel movements associated with mucus

<sup>a</sup>Percentage coded "yes" for each Manning criterion.

<sup>b</sup>Point-biserial correlation of each criterion with IBS.

<sup>c</sup> $P < 0.05$ .

<sup>d</sup> $P < 0.01$ .

<sup>e</sup>Significant  $\chi^2$ :  $P < 0.01$ .

group: there was no significant difference, however, between male and female dropouts where the scores, respectively, were 1.59 (SD, 0.16) and 1.75 (SD, 0.27).

### Procedure

The six symptoms were recorded, along with other data, on a form completed by the physician immediately after interviewing and examining the patient. Indicated diagnostic studies were ordered, available laboratory data were reviewed, and all information was recorded in a dictated evaluation. The patient was followed up at least until the diagnosis was made, usually in two or three visits, although long-term follow-up continued in many cases. Nine months after the first visit, patients were contacted by a trained research assistant who performed a structured interview via telephone to inquire about multiple dimensions that could reflect possible change in their health status; of the 97 subjects, 90 were contacted. When a physician, either the clinic gastroenterologist or another physician, had been involved in the patient's care beyond the initial diagnostic period, information was obtained directly from the physician to corroborate the patient's report.

### Analysis

Correlations were used to show the overall and simple main effects of the Manning criteria with IBS. The possibility of an interaction between gender and the Manning criteria was tested using moderated multiple regression. A significant interaction effect indicates moderation, which means that a relationship between two variables (Manning criteria and IBS) differs as a result of the level of a third variable (gender) (16). The exact nature of the differences in the relationship is revealed by the simple main effects.

### Results

For the total sample of 97 patients, the correlation of the Manning criteria with IBS was 0.22 ( $P < 0.01$ ). In the 61 women, there was a significant correlation also ( $r = 0.47$ ;  $P < 0.01$ ). In the 36 men, however, the correlation between the Manning criteria and IBS was in the opposite direction and nonsignificant ( $r = -0.16$ ). A test for a gender by Manning interaction effect, using moderated multiple regression, was significant (change in  $R^2 = 0.126$ ;  $P < 0.01$ ). Figure 1 depicts a cross-over interaction with the Manning criteria positively related to IBS for women but nonexistent for men. These results parallel the correlations described above. The Manning criteria were split at the median in the figure for illustrative purposes; the interval scale was used for the statistical test.

There was no significant difference between men and women on the six Manning criteria combined,

( $t_{95} = 1.31$ ,  $P = \text{NS}$ ). Table 1 gives the percentage of men and women coded "yes" for each of the six Manning criteria. Only one criterion was significantly associated with gender, i.e., visible abdominal bloating. Table 1 also shows the point-biserial correlation coefficient by gender for each Manning criterion with IBS. In women, three of the Manning criteria were significantly correlated with IBS (more frequent stools, looser stools, and incomplete evacuation). It is of interest, however, that not one Manning criterion correlated significantly with IBS in men. In fact, two Manning criteria, frequent bowel movements and mucus, were significantly correlated with organic disease.

As part of the previously reported study, which describes the procedure in greater detail (15), multiple demographic, descriptive, organic disease, medication, and psychosocial variables were also obtained. The psychosocial variables, along with the Manning criteria, were the hypothesis-testing variables. Psychosocial variables were not associated with IBS (15). Of these many variables, only the following were positive (with  $P < 0.01$ ): in women, constipation, pain in low abdomen, and use of bulking agents correlated positively with IBS, and a history of diarrheal symptoms in the family correlated positively with organic disease; in men, only a higher educational status was correlated positively with IBS ( $r = 0.41$ ), whereas a history of diarrhea and blood in the stool correlated negatively ( $r = -0.39$  and  $-0.43$ , respectively). The paucity of findings indicates that additional and presumably more meaningful variables will require consideration in future research. Complete data sets are available from the authors.

### Discussion

This study showed that there were significant gender differences when applying the Manning criteria in the diagnosis of IBS. The critical finding in the study was the interaction effect (Figure 1) that indicated that the Manning criteria acted differently for the two sexes. In light of this significant finding, power was sufficient.

Consistent with previous work, our study found that the Manning criteria were associated with the presence of IBS for the total study sample (2,3). However, this finding was attributable to the approximately two thirds of subjects who were women. In men, there was no correlation of the Manning criteria and a diagnosis of IBS, a finding not previously reported. However, no comparison can be made with earlier cited studies, because gender effects on the diagnosis of IBS were not evaluated (2,3). Although gender differences were not the focus in a recent study by Talley et al., a very brief reference suggests limited

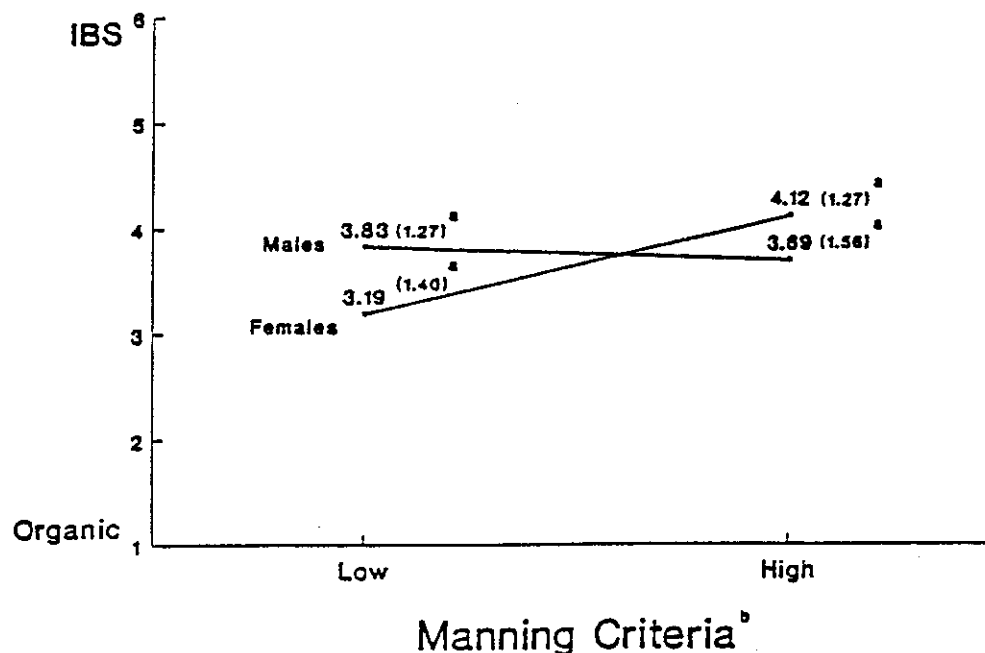


Figure 1. Gender by Manning criteria interaction in diagnosis. <sup>a</sup>SD in parentheses; <sup>b</sup>high and low scores refer to fulfillment of Manning criteria with split at median.

value of the Manning criteria in men (17). Their self-report questionnaire methodology differed from the current study, which used gastroenterologists to elicit the Manning criteria; this could account for disparate findings. Additional studies designed to test gender differences are clearly required.

The dropout group had significantly higher scores on the Manning criteria than the study sample, but they dropped out in roughly the same proportion. It is unlikely from a statistical standpoint that addition of the 11 men in this group would reverse the present trend toward a negative relationship and support the use of the Manning criteria as predictors of IBS in men. Rather, assuming that a linear relationship existed, the effect size would increase and therefore increase the probability that the now nonsignificant negative correlation would become significant. Most likely, however, is that there would be no change in what appears now to be a nonsignificant relationship. Thus, the restriction of range associated with higher Manning scores in the dropout group is not likely to affect the findings in this study.

Gender differences are well known to occur in many dimensions of medicine (9-12). Although their discussion is outside the purview of this paper, it merits brief comment that IBS has been shown to be more common in women, both in those seeking health care (3,6,7) and in those who do not (18,19). Further, the general process of somatization is believed by some to be different in men and women (20).

This study corroborated the diagnostic value, albeit limited, of the Manning criteria for the two thirds of patients with IBS who are women, a finding also recently confirmed by Whitehead et al. (21). Unfortu-

nately, the study also highlights that the smaller subset of patients with IBS who are men perhaps cannot be satisfactorily diagnosed using the Manning criteria. We concluded that, in particular for men, the only reliable diagnostic tool for diagnosing IBS is laboratory and other investigation. Future research will have to answer whether there are different markers for IBS in men or if what is now called IBS in men is perhaps a different disorder.

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