

Fibromyalgia in the Irritable Bowel Syndrome: Studies of Prevalence and Clinical Implications

A. D. Sperber, M.D., M.S.P.H., Y. Atzmon, M.D., L. Neumann, Ph.D., I. Weisberg, M.D., Y. Shalit, M.D., M. Abu-Shakrah, M.D., A. Fich, M.D., and D. Buskila, M.D.

Departments of Gastroenterology, Epidemiology, and Rheumatology, Soroka Medical Center and Faculty of the Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva, Israel

OBJECTIVE: The irritable bowel syndrome (IBS) and the fibromyalgia syndrome (FS) coexist in many patients. We conducted complementary studies of the prevalence of FS in IBS patients and matched controls, and of IBS in FS patients and the implications of concomitant IBS and FS on health-related quality of life (HRQOL).

METHODS: A study of 79 IBS patients with 72 matched controls (IBS study), and a study of 100 FS patients (FS study). All participants underwent tests of tender point sites and threshold of tenderness and answered questionnaires including personal and medical history, GI symptoms, and indices of HRQOL.

RESULTS: In the IBS study, 25 of the 79 IBS patients (31.6%) and 3 of the 72 controls (4.2%) had FS ($p < 0.001$). Statistically significant differences were found among the study groups in terms of global well-being ($p < 0.001$), sleep disturbance ($p < 0.001$), physician visits ($p = 0.003$), pain ($p < 0.001$), anxiety ($p < 0.001$), and global severity index (SCL-90-R) ($p < 0.001$), with patients with IBS and FS having the worst results. IBS patients had significantly more tender points than controls ($p < 0.001$). In the FS study, 32 of the 100 FS patients (32%) had IBS. Patients with both disorders had significantly worse scores for physical functioning ($p = 0.030$) and for all but one of a 16-item quality of life questionnaire.

CONCLUSIONS: FS and IBS coexist in many patients. Patients with both disorders have worse scores on HRQOL indices than patients with either disorder alone, or controls. Physicians treating these patients should be aware of the overlap, which can affect the presentation of symptoms, health care utilization, and treatment strategies. (Am J Gastroenterol 1999;94:3541–3546. © 1999 by Am. Coll. of Gastroenterology)

INTRODUCTION

The fibromyalgia syndrome (FS) is a soft tissue disorder characterized by diffuse musculoskeletal pain and specific tender points on examination. Many FS patients have concomitant functional disorders, including the irritable bowel syndrome (IBS) (1–8). It has been suggested that these and

other functional disorders, such as migraine headaches, chronic fatigue, chronic dizziness, and irritable urinary bladders, may represent a group of illnesses sharing a common pathogenesis (2, 7, 9, 10). No comprehensive, controlled study has been published on the prevalence and significance of concomitant IBS and FS.

IBS is the prototypical functional disorder of the GI tract. Patients suffer from chronic abdominal pain and disturbed bowel function without evidence of structural or laboratory abnormalities on routine testing (11, 12). The estimated prevalence of IBS in the adult populations of Western countries ranges from 12–20%, and it is more prevalent among women (13–18). As many as 28% of referrals for gastroenterology consultations are for IBS (19). Consensus diagnostic criteria for IBS and the other functional GI disorders, the Rome criteria, have been established (11, 12). These criteria are particularly important for defining patient populations for research purposes, such as epidemiological and quality of life studies, as well as therapeutic clinical trials.

We conducted parallel studies of the prevalence of FS among IBS patients compared with matched controls (“IBS study”), and the prevalence of IBS among FS patients (“FS study”). We also evaluated the implications of the association between these functional entities on clinical and health-related quality of life (HRQOL) indices (20), because these measurements are particularly applicable to conditions in which the subjective perceptions of the patient are of critical importance to the course of the illness. The demonstration of significant associations between these entities could have a bearing on studies of common pathophysiological mechanisms and therapeutic strategies.

MATERIALS AND METHODS

IBS Study

Seventy-nine patients with IBS, diagnosed by the Rome criteria (11, 12) and 72 controls, matched by age and gender, participated in the study. All the patients were enrolled from the GI clinic of the Soroka Medical Center in Beer-Sheva, Israel. All patients had been followed in the GI clinic for at least 1 yr before enrollment, and all had previously undergone appropriate work-up to establish the diagnosis. Partic-

ipation in the study was proposed to all patients at routine visits to the clinic and those who agreed were enrolled after receiving full information on the study and signing informed consent forms. The controls were all volunteers recruited by convenience from the general and medical staffs of the medical center, from the workers and staff of the Ben-Gurion University of the Negev, and from neighboring towns and kibbutzim. All participants completed a self-administered questionnaire that included sociodemographic background, a medical history, GI symptomatology including standardized questions for diagnosis of IBS in accordance with the Rome criteria, general well-being, health care use (physician visits, hospitalizations, operations), psychological distress (SCL-90 symptom checklist) (21, 22), and an anxiety state index (23). For the SCL-90, the Global Severity Index (a mean of all 90 questions), and the nine subscales (somatization, obsessive/compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism) were calculated. The IBS patients (but not the controls) also completed a questionnaire on their concerns related to their illness. This questionnaire (RFIPC) was originally designed for patients with inflammatory bowel disease (24). A global score and four subscores (concerns on (1) impact of disease on life, (2) complications, (3) sexual intimacy, and (4) body image) were calculated. The Hebrew version of the entire questionnaire was validated by a method developed and published by one of the authors (25).

FS Study

One hundred female FS patients, chosen at random from a list of 500 FS patients attending the Rheumatology Clinic of the Soroka Medical Center, were included in the second arm of the study. Visual analog scales were used to evaluate current levels of pain, anxiety, depression, fatigue, morning stiffness, and global well-being. In addition, subjective reports of the presence or absence of symptoms such as sleep disturbance, dizziness, headache, and paresthesias were recorded. Quality of life was assessed in these patients with a 16-item questionnaire adapted by Burkhardt *et al.* (26) from an earlier instrument by Flanagan (27). The Hebrew version of the instrument has been validated (28). Physical functioning was assessed by questions 1 to 10 of the Fibromyalgia Impact Questionnaire (29), which has also been validated in Hebrew (30).

In both studies FS was diagnosed if patients fulfilled the American College of Rheumatology criteria of 1990 (31) namely, widespread pain in combination with tenderness of 11 or more of the 18 specific tender point (TP) sites. A count of 18 TP at nine symmetrical sites was performed by thumb palpation. Manual pressure was demonstrated at a control site first. Patients were told to expect a sensation of pressure but to indicate if this became painful. Definite tenderness at any point was considered to be present if some involuntary verbal or facial expression of pain occurred or a wince or

withdrawal was observed. The amount of manual pressure applied over a TP was about 4 kg/cm² (tested periodically against a dolorimeter).

Thirteen point sites (nine TP sites and four control sites) were further studied for threshold of tenderness with a Chatillon dolorimeter, model 719-20, which has a maximum scale of 9 kg, with a neoprene stopper as footplate and a diameter of 1.4 cm (32). The site of maximum tenderness over TP sites was determined by preliminary light pressure. The footplate of the dolorimeter was then placed appropriately, and if necessary, its location was stabilized with the examiner's nondominant hand to prevent (often painful) shifting of the footplate under pressure, taking care not to add or subtract from the force applied. The dolorimeter was held close to the vertical position. Pressure was increased at the rate of about 1 kg/s. The subject was asked to say "yes" when the sensation no longer was pressure, and became definite pain. Preliminary measures of control sites were done to familiarize the subject with the process, but also to discourage anticipation or exaggerated responses. All dolorimeter measurements of 13 point sites as well as a total point count were done by one observer. A detailed description of the point sites is presented elsewhere (30). All tests were done by the same examiner in each study.

Statistical Analyses

Data were analyzed using the JMP software (SAS for Macintosh) for the IBS study, and SPSS (Statistical Package of the Social Sciences, Chicago, IL) for the FS study. The χ^2 statistic or *t* tests and analysis of variance were used, as appropriate, for comparison of proportions or means. Posthoc Tukey-Kramer HSD tests were performed, when appropriate. Statistical significance was set at $p < 0.05$ throughout. Means are reported as \pm SD.

Subgroup Analyses

In the IBS study, separate analyses were conducted for the following compositions of patients (Fig. 1A,B): (1) the original study groups of 79 IBS patients and 72 matched controls ("study" groups); (2) 23 of the controls had IBS on the basis of the questionnaire. These were grouped separately into a "IBS nonpatient" group. Comparisons were done for 79 IBS patients, 23 IBS nonpatients, and 49 healthy controls ("functional status" groups; Fig. 1A); (3) 25 of the 79 IBS patients had FS and IBS. These were grouped separately into a coexisting IBS and FS group, which was compared with the 54 patients who had IBS only, and the 72 controls ("fibromyalgia status" groups; Fig. 1B).

The Internal Review Board (Helsinki Committee) of the Soroka Medical Center approved the study.

RESULTS

IBS Study

Seventy-nine IBS patients and 72 matched controls completed the study. There were no significant differences be-

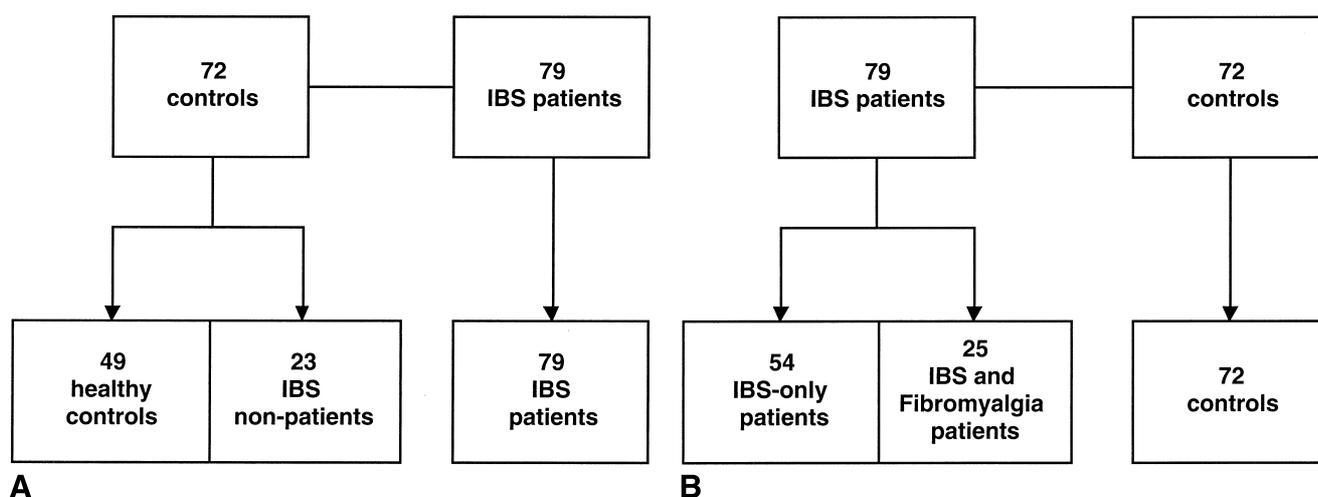


Figure 1. Study design for subgroup analyses: (A) “functional status” groups, (B) “fibromyalgia status” group.

tween the groups in age (mean age 47.1 ± 14.5 yr for IBS and 46.0 ± 15.4 yr for controls), gender (77% of IBS patients and 75% of controls were women), or other socio-demographic variables.

PREVALENCE OF FIBROMYALGIA. Twenty-five of the 79 IBS patients (31.6%) and 3 of the 72 controls (4.2%) had FS ($p < 0.001$). By functional status, 25 of 79 IBS patients (31.6%), 1 of 23 IBS nonpatients (4.3%), and 2 of other 49 controls (4.1%) had FS ($p < 0.001$).

MEASUREMENTS OF TENDERNESS. The mean number of tender points (of 18 tested) was 7.5 ± 5.5 for the IBS patients and 2.5 ± 3.6 for the controls ($p < 0.001$). By functional status, the mean number of tender points was 7.5 ± 5.5 for the IBS patients ($n = 79$), 2.9 ± 4.0 for the IBS nonpatients ($n = 23$), and 2.3 ± 3.3 for the other control patients ($n = 49$) ($F = 21.0$, $df = 2; 146$, $p < 0.001$).

The mean dolorimeter tenderness threshold at nine tender point sites was 4.5 ± 2.0 kg for the IBS group and 7.4 ± 1.4 kg for the controls ($p < 0.001$). The 25 IBS patients with

coexisting FS had a dolorimeter score of 2.6 ± 1.0 kg, which was significantly lower than the corresponding score of 5.4 ± 1.7 kg for the 54 IBS patients who did not have FS ($p < 0.001$).

QUALITY OF LIFE, PSYCHOLOGICAL STATUS, AND HEALTH CARE UTILIZATION. There was a statistically significant gradient of severity from controls, to IBS nonpatients, to IBS-only patients, to IBS patients with concomitant FS (Table 1). The only variable for which no significant difference was found between patients with IBS and controls was the number of hospitalizations over the past year. Hospitalization in the Soroka Medical Center is not affected by bed availability, and thus is available for any patient as determined by the emergency room staff or by physicians affiliated with the hospital. In all variables with significant differences we found additional differences between IBS-only patients and patients with IBS and FS. Table 2 shows the subscale results for the SCL-90R and the Concerns indices.

Table 1. Comparison of Health-Related Quality of Life Variables, by Subgroups (mean \pm SD)

	Controls (A) n = 49	IBS Nonpatients (B) n = 23	IBS-only (C) n = 54	IBS/FS (D) n = 25	p Value*	Post-hoc Test Tukey-Kramer
Global feeling (1 = best; 10 = worst)	1.1 \pm 1.8	1.6 \pm 2.0	3.7 \pm 2.6	5.2 \pm 2.3	<0.001	C vs A + B D vs A + B
Sleep disturbance	22.4%	22.7%	46.3%	64.0%	<0.001	D vs A + B
Physician visits over past year (n)	1.0 \pm 1.3	1.8 \pm 2.6	3.7 \pm 6.0	7.7 \pm 13.7	<0.001	D vs A + B
Are symptoms stress-related?	Not in questionnaire		75.5%	82.6%	0.040	
Hospitalizations over past year (n)	0.19 \pm 0.7	0.19 \pm 0.5	0.19 \pm 0.7	0.13 \pm 0.5	NS	—
Abdominal pain (VAS) (1 = least pain; 100 = worst pain)	1.9 \pm 6.7	12.7 \pm 18.6	31.3 \pm 28.4	50.1 \pm 21.9	<0.001	D vs A, B + C C vs A + B
Anxiety (1 = least; 4 = most)	1.7 \pm 0.4	1.9 \pm 0.5	1.9 \pm 0.5	2.4 \pm 0.6	<0.001	D vs A, B + C
Global severity index (SCL-90R) (0 = least; 4 = most)	0.5 \pm 0.5	0.7 \pm 0.6	0.9 \pm 0.6	1.3 \pm 0.8	<0.001	D vs A, B + C C vs A
Concerns (mean of 25 items) (0 = least; 100 = most)	Not in questionnaire		25.2 \pm 16.4	36.0 \pm 17.4	0.010	

* ANOVA when three means are compared, t-test when two means are compared, and χ^2 when proportions are compared.

Table 2. Subscales of Concerns Questionnaire and SCL-90R, by Subgroups (mean \pm SD)

	Controls (A) n = 49	IBS Nonpatients (B) n = 23	IBS-only (C) n = 54	IBS/FS (D) n = 25	p Value	Post-hoc Test Tukey-Kramer
Concerns (0 = least, 100 = most)						
Impact of disease		Not in questionnaire	30.8 \pm 16.4	45.5 \pm 20.4	<0.001	
Complications		Not in questionnaire	21.8 \pm 26.7	28.6 \pm 27.6	NS	
Sexual intimacy		Not in questionnaire	23.5 \pm 23.9	38.7 \pm 32.9	0.020	
Body image		Not in questionnaire	15.8 \pm 27.1	19.4 \pm 28.7	NS	
SCL-90R (0 = least, 4 = most)						
Somatization	0.5 \pm 0.5	0.7 \pm 0.7	1.1 \pm 0.7	1.8 \pm 0.7	<0.001	D vs A, B + C C vs A
Obsessive/compulsive	0.8 \pm 0.7	0.9 \pm 0.9	1.0 \pm 0.8	1.4 \pm 0.9	0.040	D vs A
Interpersonal sensitivity	0.7 \pm 0.7	0.8 \pm 0.8	0.9 \pm 0.7	1.3 \pm 0.8	<0.01	D vs A
Depression	0.7 \pm 0.6	0.8 \pm 0.8	1.0 \pm 0.8	1.4 \pm 0.9	<0.05	D vs A + B
Anxiety	0.4 \pm 0.5	0.6 \pm 0.6	0.8 \pm 0.7	1.4 \pm 0.7	<0.01	D vs A, B + C C vs A
Hostility	0.5 \pm 0.5	0.5 \pm 0.6	0.8 \pm 0.7	0.9 \pm 0.9	<0.001	D vs A
Phobic anxiety	0.3 \pm 0.7	0.4 \pm 0.6	0.6 \pm 0.7	0.8 \pm 0.9	0.05	D vs A
Paranoid ideation	0.5 \pm 0.6	0.7 \pm 0.9	0.8 \pm 0.9	1.0 \pm 1.0	NS	NS
Psychoticism	0.4 \pm 0.7	0.4 \pm 0.4	0.6 \pm 0.7	0.8 \pm 0.6	NS	NS

NS = not significant.

FS Study

One hundred women with FS participated in the study.

PREVALENCE OF IBS. Thirty-two of the patients had evidence of IBS (32%). The mean age of the women with FS only and those with FS and IBS was 48.6 \pm 14.9 yr and 48.5 \pm 10.8 yr, respectively. There were no significant differences between the two groups in sociodemographic variables.

MEASUREMENTS OF TENDERNESS. The mean number of tender points was significantly higher in patients with FS and IBS compared to those with FS only, although by definition all, as FS-diagnosed patients, had at least 11 of 18 tender points. The mean for patients with FS and IBS was 15.6 \pm 2.5 compared to 14.1 \pm 2.7 for those with FS only ($p = 0.008$). There were no differences between the groups in dolorimeter thresholds at the nine tender points (1.6 \pm 0.6 kg and 1.7 \pm 0.6 kg, respectively), or at the four control points (3.6 \pm 0.8 kg and 3.8 \pm 0.7 kg, respectively).

QUALITY OF LIFE, PSYCHOLOGICAL STATUS, AND HEALTH CARE UTILIZATION. Most of the patients reported sleep disturbances, 82.4% for FS alone and 87.1% for patients with FS and IBS. There were no significant differences in the visual analog scale report of pain or global well-being. Significant differences were found between these groups in terms of pain interrupting work ($p < 0.005$), fatigue ($p = 0.039$), and morning tiredness ($p = 0.020$). In all cases the patients with both FS and IBS had the worse score. Patients with both disorders rated their FS as more severe (8.8 \pm 1.5 compared to 8.0 \pm 2.0, $p = 0.052$).

On the physical functioning questionnaire, patients with both FS and IBS reported significantly more problems in cooking ($p = 0.040$), dishwashing ($p = 0.020$), making the bed ($p = 0.010$), and social visits ($p = 0.020$). There were

no areas in which those with FS only reported more problems. The mean sum score for physical functioning (0 = best, 3 = worst) was 1.5 \pm 0.6 for FS only and 1.8 \pm 0.8 for both FS and IBS ($p = 0.030$).

On the 16-item quality of life questionnaire, patients with both FS and IBS had worse scores for all but one item. For four items, general health, work, sports, independence, the differences between the groups were significant, in all cases to the detriment of the patients with both FS and IBS. The overall quality of life scores (1 = worse, 7 = better) were 3.3 \pm 1.0 for patients with both disorders compared to 3.8 \pm 1.2 for patients with FS only ($p = 0.060$).

DISCUSSION

To our knowledge this is the most comprehensive study of the association between IBS and FS. Previous studies have assessed the prevalence of IBS in patients with FS (1–8), and one other study assessed the prevalence of each disorder in patients diagnosed with the other, but the patient groups were smaller (7). Estimates of the prevalence of IBS in patients with FS range from 30 to 35% (1, 6) to as high as 70% (7). In those studies in which controls were also tested, the prevalence of IBS was in the range of 8–16% (5–7).

The strong association of IBS and FS has raised the question of a possible common pathogenesis, perhaps with other functional disorders (2, 7, 9, 10). This issue has generated controversy in that the basic mechanism of pathology of IBS can be thought of as psychopathology (2, 33) or, in contrast, as aberrations of central pain mechanisms involving neuroendocrine, and possibly immune system dysfunction (9).

Although stress and psychological morbidity are often associated with IBS and FS, they are not the cause. However, they do have an effect on patients' perceptions of their illness and a modulating effect on the clinical course and

outcome. An important finding, in this respect, is that not all individuals with IBS seek consultations or professional health care. Some individuals (referred to as IBS nonpatients), fulfill the Rome criteria for IBS on the basis of their answers to survey questionnaires, but do not seek medical care for their symptoms. They are more similar to healthy controls than to IBS patients in indices of health-related quality of life including psychological profiles, daily functioning, and health care utilization. The existence of this prevalent group (about 12–20% of the general adult population) emphasizes the perception that IBS is not a psychological illness, but that psychosocial factors modulate the expression of the symptoms in terms of coping, health care utilization, and quality of life. In our control group there was a relatively high percentage of IBS nonpatients (31.9%). We have no specific explanation for this finding, which may stem from the demographic makeup of this group. This finding can only affect the results of the study by introducing a conservative bias, as theoretically it could lead to a higher prevalence of FS in the control group. This, however, was not the case.

In the present study we were able to assess the relative prevalence of FS in IBS patients and controls, and the prevalence of IBS in FS patients, using strict diagnostic criteria. FS was diagnosed in 31.6% of the IBS patients compared to 4.3% of the IBS nonpatients and 4.2% of the other controls. IBS was diagnosed in 32% of the women with FS. The prevalence of FS among IBS patients was not affected “psychologically” by the severity of IBS symptoms. Although the IBS patients with FS had a higher Functional Bowel Disorder Severity Index score than those without FS (138.8 ± 157.6 vs 81.4 ± 71.2 , respectively), the diagnosis of FS was based on tender points and threshold measurements and not on the patients’ report of FS symptoms. The design of the IBS study further enabled us to compare health-related quality of life indices and psychological distress profiles among IBS-only patients, IBS nonpatients, patients with IBS and FS, and healthy controls.

The findings of our study were universally consistent. The IBS nonpatients were more similar to the other controls than to the IBS patients, although their results were consistently in between the patients and the other controls. When patients with both FS and IBS were compared with those with IBS-only and controls, a graded severity was again observed, in which controls had the most favorable results and the 25 patients with both entities had the worst. All of the parameters tested showed statistically significant differences among the groups, except for the number of hospitalizations during the past year. This is interesting in light of the significant difference in the number of physician visits over the same year. The IBS-only patients and the patients with both IBS and FS visited their physicians considerably more than IBS nonpatients or other controls, but did not require hospitalization for their complaints. This finding is also consistent with the finding that patients with IBS and FS

were not more concerned about possible complications of their disease than those with IBS-only. Thus, despite the significant number of physician visits and the impaired quality of life in patients with IBS and FS, they are not hospitalized more frequently and are not more concerned about possible future complications of their disease.

Our study did not touch on the possible physiological mechanisms common to or different in FS and IBS. Recent studies have implicated visceral afferent hypersensitivity as a putative factor in IBS (34). In contrast, somatic hypersensitivity may be predominant in FS. Recent studies of visceral and somatic sensitivity in IBS and FS patients have yielded contrasting results. One study concluded that rectal visceral afferent hyperalgesia may be similar in the two patient groups and thus nonspecific for IBS (35). In contrast, another study concluded that these groups have different nociceptive responses (1) and may have different supraspinal processing of visceral and somatic aversive stimuli (36). We found significantly more tender points in IBS patients than controls. We also found that IBS nonpatients had the same mean number of tender points as other controls, which was significantly less than the number of tender points in IBS patients. In addition, patients with FS and IBS had significantly more tender points than those with FS only, although FS patients, by definition, have at least 11 tender points of the 18 tested. Thus, there are clear differences in a physical test of tenderness between IBS patients and IBS nonpatients, and between patients with FS alone or with both FS and IBS. The difference in tenderness may represent somatic hypersensitivity in a subset of IBS patients, may be related to the psychological differences between the groups, or may reflect a difference in their central processing of noxious stimuli. The use of antidepressants as central analgesics for both IBS and FS patients lends credibility to the possibility of a common underlying mechanism of pain sensitivity or processing.

Our observations on the association between IBS and FS are clinically relevant to physicians who care for patients with IBS or FS, or both. The tender point count required for the diagnosis of FS requires minimal training and takes only a few minutes to perform. It can be carried out easily by gastroenterologists and other nonrheumatologists. The diagnosis of IBS can be learned easily by nongastroenterologists. Increased awareness of the clinical impact of FS on IBS patients and vice versa, and recognition of the implications of this association for quality of life, should enable physicians to reassure their patients as to the nature and severity of their symptoms, and to provide appropriate treatment. This may lead to a reduction in unnecessary tests and referrals for these patients.

The existence of a subset of IBS patients with somatic hypersensitivity may have implications for the understanding of the pathogenesis of IBS and potential therapeutic approaches. Thus, it warrants further studies.

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Reprint requests and correspondence: Ami D. Sperber, M.D., M.S.P.H., Department of Gastroenterology, Soroka Medical Center, Beer-Sheva, Israel 84101.

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