Fibromyalgia

Recognition and Management in the Primary Care Office

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KEYWORDS

• Fibromyalgia • Depression • Fatigue • Sleep • Nonpharmacological interventions

KEY POINTS

- Fibromyalgia is a chronic pain disorder resulting from abnormal central sensitization and a chronic stress pattern of response.
- There is no evidence that fibromyalgia is an inflammatory/autoimmune disorder.
- The diagnosis of fibromyalgia is clinically based on a combination of symptoms such as generalized pain, fatigue, nonrestorative sleep, cognitive difficulties, and associated conditions such as irritable bowel syndrome and migraines. Psychological/psychiatric comorbidities are common.
- The evaluation of fibromyalgia should include assessment of mood, sleep, level of exercise, patient maladaptive responses to pain and stressors, and past and present stressors.
- The current available drugs have very limited benefit. The treatment must be individualized and focused on modifying reversible factors: maladaptive responses via psychological interventions, regular exercise, treatment of psychiatric comorbidities, and improvement of sleep.

INTRODUCTION

The medical literature, going back to the nineteenth century, includes numerous writings about what we call today fibromyalgia syndrome (FMS). In 1880, George Miller Beard, an American neurologist described nervous exhaustion or neurasthenia[1] as a medical condition caused by the exhaustion of the central nervous energy reserves, characterized by fatigue, anxiety, headache, depression, shooting pains, local spasms of muscles, and numerous other symptoms that he painstakingly elaborated on over the span of 75 pages. In 1904 Sir William Gowers, a British neurologist, coined the name “fibrositis” for a type of spontaneous back pain occurring without evidence

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for inflammation, aggravated by cold and exertion and associated with sensitivity to mechanical compression, fatigue, and sleep disturbances.[2] Studies of Second World War soldiers reported on "psychogenic rheumatism" and fibrositis as conditions associated with "hysterical features" and "tender localized areas or nodules"[3] intensified and perpetuated by mental influences and persistence despite prolonged bed rest.[4]

Mohammed Yunus used the term "fibromyalgia syndrome" interchangeably with fibrositis to describe the combination of chronic pain, fatigue, stiffness, and poor sleep as a form of nonarticular rheumatism associated with increased tenderness in specific anatomic sites called trigger points.[5]

Fast forward to now, FMS is still defined by its clinical symptoms,[6] largely because the central and peripheral mechanisms of chronic pain are not well understood. Martinez-Lavin described FMS as a stress-related condition resulting from a "failed attempt of our main complex adaptive system to accommodate to a hostile environment."[7] Hans Selye defined stress as a nonspecific response of the body to any demand and coined the term "distress" to describe maladaptive responses to stress leading to somatic and psychological harm.[8] Later Lazarus and Folkman[9] emphasized that the appraisal of a situation, as threatening is important for triggering the stress response with activation of the sympathetic nervous system (fight or flight response) and of the hypothalamic-pituitary-adrenal axis. Several methods of measuring the activation of the sympathetic nervous system such as heart rate variability analysis, tilt table testing, and sympathetic skin response have shown evidence of overactivity in FMS.[10] Both physical (war trauma, surgery, accidents, illnesses, pregnancy and birth, physical abuse) and emotional stressors (sexual and mental abuse, conflict, neglect, divorce) as well as ongoing stressful life events (financial, job, social, family, illness related) have shown long-lasting changes in pain sensitivity, likely via the engagement of the stress response and epigenetic alterations.[11] The exact mechanism of how the activated stress response leads to chronic pain needs further study. Clinical studies show that maladaptive stress responses such as catastrophizing, passive coping strategies, harm avoiding personalities, and depressed and anxious mood perpetuate the stress response, which may contribute to the chronicity of pain.[12] Most recently FMS has been defined as a primary pain syndrome rather than a nociceptive process in the musculoskeletal system[13] largely due to extensive evidence of abnormal brain pain processing[14] and brain connectivity[15] along with malfunction of descending pain inhibitory pathways.[16] Brain studies using functional MRI showed that patients with FMS experience pain and activate brain pain processing areas when exposed to pressure stimuli that are not painful in healthy controls.[14] There is also evidence that peripheral mechanisms may contribute to FMS symptoms such as myalgias and "neuropathic" complaints. Although no structural or inflammatory abnormalities have been observed in peripheral muscles, there is evidence for decreased numbers of small fibers in the skin in patients with FMS[17] and increased levels of glutamate, pyruvate, and lactate in the muscles of patients with FMS that may contribute to the increased pain.[18] This does not rule out the primary nature of FMS pain, as these findings may be the effect of a chronic amplified stress response leading to chronic tissue ischemic changes.

PREVALENCE OF FIBROMYALGIA SYNDROME AND GENDER DISTRIBUTION

The FMS prevalence in the general population is reported between 2% and 10%[19–21] depending on the population studied and the criteria used of diagnosis. Fibromyalgia clinical cohorts often report up to 90% female predominance likely because women are more prone than men to self-refer for care, they have more tender points, and often

report more symptoms than men.[22] General population studies using American College of Rheumatology (ACR) diagnostic criteria show ratios of women/men of 6.8 (ACR 1990)[7] to almost equal prevalence (ACR 2016).[10]

DIAGNOSTIC CRITERIA FOR FIBROMYALGIA

The criteria for the diagnosis of FMS have evolved over time.[23–28] The widely used 1990 ACR criteria were focused solely on wide spread pain and the presence of a sufficient number of tender points.[24] Over time the criteria have evolved in several important ways: (1) inclusion of other core FMS symptoms such as fatigue, sleep, and cognitive difficulties; (2) elimination of tender point counts; and (3) allowing exclusively patient completed questionnaires to determine if FMS criteria are met, eliminating the need for a physician input[27] (**Table 1**).

WHEN SHOULD FIBROMYALGIA SYNDROME BE SUSPECTED IN CLINIC?

The diagnosis of FMS is clinical and is often suggested by a "pan positive" review of systems. The core symptoms of FMS are generalized aches and pains often worse with cold and humidity, fatigue, and nonrestorative sleep.[28,29] Other common symptoms are tenderness to touch, stiffness, dryness of mouth and/or eyes, headaches, dizziness, temporomandibular joint complaints, nausea, abdominal pain and bloating, diarrhea often alternating with constipation, frequent urination at night, sensations of subjective swelling, intermittent paresthesias, and environmental sensitivity[5,30] (**Table 2**). Classification criteria for FMS require a minimum of 3 months of symptoms, but most of the patients had symptoms for years, so physicians should be cautious diagnosing FMS in patients with short duration of symptoms, as none of these symptoms are specific for FMS and consider potential "red flags" that may suggest other conditions (**Table 3**). The tenderness to touch defined as sensitivity of soft tissues and muscles to pressure that would not normally cause pain[28] may help differentiate FMS from other inflammatory conditions. About 80% of FMS patients have tender points (areas of increased pain with a standardized pressure of 4 kg/cm^2) on palpation, more often women than men.[22] In 1997 Frederick Wolfe proposed that the tender point count is akin to a "sedimentation rate" for distress and that both fibromyalgia symptoms and tenderness are part of a continuum of distress, rather than discreet diagnostic markers for FMS.[31] The presence of tender points on physical examination is no longer a requirement for diagnosis.[25]

It is not uncommon for patients to resist the passive range of motion and exhibit limited by pain forward lumbar flexion. Occasionally patients also have brisk deep tendon reflexes, cold and purplish discolored extremities, and occasionally a livedoid pattern triggered by cold exposure called cutis marmorata.

COMMON MEDICAL AND PSYCHIATRIC COMORBIDITIES IN FIBROMYALGIA SYNDROME

Patients with FMS are often diagnosed with other conditions presumed to share the common pathophysiology of central sensitization: chronic fatigue, irritable bowel syndrome, pelvic pain syndrome, migraine, temporomandibular disorder, small fiber neuropathy, and interstitial cystitis.[28]

There is a high association between FMS and psychiatric conditions such as major depressive disorder, general anxiety disorder, posttraumatic stress disorder, bipolar disorder, and personality disorders.[28] By using structured clinical psychiatric

Table 1
Diagnostic/classification criteria for fibromyalgia syndrome

Authors/Citation Name	Criteria	Comments
Wolfe et al,[24] 1990 ACR 1990 FMS Classification Criteria	• Widespread pain • Tenderness at ≥11/18 tender points • Duration of symptoms ≥3 mo	Tender points (24 points, 12 symmetric areas): Upper neck and back • Suboccipital muscles insertion • Low cervical at the level of C5–7 trapezius muscles • Midscapulae Lower back and hips: • Gluteal areas • Greater trochanter areas Anterior chest: • Second rib costochondral junctions • Lateral pectorals at the level of fourth ribs Upper extremities: • Lateral epicondyles lower extremities • Medial fat pad knees
Wolfe et al,[27] 2016 ACR 2016 FMS Criteria	• Generalized pain + pain in ≥4 (out of 5) regions (pain in the jaw, chest, and abdomin are not included) • Duration ≥3 mo • WPI ≥7 and SS ≥5 or WPI 4–6 and SS≥9 • Fibromyalgianess scale = the fibromyalgia severity (FS) scale = WPI + SS; FS scale is a full component of the FMS criteria • A diagnosis of FMS is valid irrespective of other diagnoses	New: • Allows patients with less pain/localized pain extent and more somatic symptoms to be classified as FMS Regions: • Left and right upper region: jaw, shoulder girdle, upper arm, lower arm • Left and right lower region: hip, upper leg, lower leg • Axial region (neck, upper back, lower back, chest, abdomen) WPI measures presence of pain in 19 areas of the body (score 0–19) Symptom Severity (SS) scale assesses 3 key symptoms associated with FMS: fatigue, cognitive problems, and nonrestorative sleep, and other somatic complaints each on a scale from 0-3 (score 0–12)

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Table 1
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Authors/Citation Name	Criteria	Comments
		The somatic symptom list is simplified to 3 symptoms that have occurred in the past 6 mo: headaches, pain, or cramps in the lower abdomen and depression (each add 1 point if present)

Abbreviation: WPI, Widespread Pain Index.

Adapted from Wolfe F, Smythe HA, Yunus MB, et al. The American College of Rheumatology 1990 Criteria for the Classification of Fibromyalgia. Report of the Multicenter Criteria Committee. Arthritis Rheum 1990;33(2):160-172; and Wolfe F, Clauw DJ, Fitzcharles MA, et al. 2016 Revisions to the 2010/2011 fibromyalgia diagnostic criteria. Semin Arthritis Rheum 2016;46(3):319-329; with permission.

interviews, criteria for axis I psychiatric disorders were met by at least half, and almost one-third of patients with FMS met diagnosis criteria for axis II.[39] It has been shown that the severity of comorbid depression and the presence of bipolar spectrum symptoms parallel the severity of FMS.[33]

Table 2
Clinical aspects of fibromyalgia syndrome

Symptom	Characteristic Features
Pain[32]	Location: • Muscles or joints or both • The back is almost always affected, which helps differentiation from lupus or rheumatoid arthritis that do not affect the lower back Relationship with time of day: • More severe at night, in the morning Relationship with activity: • Worse with prolonged immobility and after exertion Characteristics of pain: • Described in vivid terms: "I feel I have been hit by a truck"; "I feel I have a constant flu"; the pain is "stabbing," "burning," "unbearable"
Stiffness[33]	Duration: • Often longer than 1 h • More pronounced in the morning and after immobility • Does not classically respond to low- to moderate-dose glucocorticoid therapy
Tenderness to touch[28]	• Sensitivity of soft tissues and muscles to pressure that would not normally cause pain[28]
Environmental sensitivity and hypervigilance[28]	• Sensitivity to bright lights and or loud noises and or strong smells • Intolerance to cold and or humidity

Table 3
Conditions to consider in the differential diagnosis of fibromyalgia syndrome

Condition	What Is Common with FMS	What Is Different from FMS
Rheumatoid arthritis and other inflammatory arthritides[32]	• Pain: articular, nocturnal, with rest, better with movement • Stiffness: >1 h • Fatigue • Night sweats ??	• Objective evidence for swollen joints • Abnormal radiographic changes (erosions, chondrocalcinosis) • Lack of low back involvement in rheumatoid arthritis • Elevated markers of inflammation and positive serologies: C-reactive protein, Westergren sedimentation rate, rheumatoid factor, cyclic citrullinated peptide antibodies
Polymyalgia rheumatica/ giant cell arteritis[34]	• Pain in neck, upper back, arms, thighs, gluteal area • Stiffness>1 h • scalp sensitivity • Fatigue • Night sweats • Tenderness with palpation over affected areas	• Occurs after age 50 y, often in the 70s • Duration of symptoms of relatively short duration (days, weeks, rarely months) before seeking care • Elevated markers of inflammation • Dramatic response to glucocorticoid therapy • Positive temporal artery biopsy
Inflammatory myositis/ dermatomyositis/overlap syndromes/antisynthetase syndrome[35]	• Subjective sense of weakness • Fatigue	• Objective evidence for weakness, proximal and or distal • Lack of myalgias or minimal muscular pain • Elevated creatine kinase (often in the thousands) • Other objective findings: interstitial lung disease, skin rash, periungual changes, occasionally inflammatory arthritis, Raynaud phenomenon
Peripheral neuropathy[36]	• Shooting burning pain • Paresthesias • Numbness • Weakness	• Abnormal neurologic examination • Abnormal EMG
Addison disease[36,37]	• Fatigue • Postural hypotension • Nausea • Vomiting	• Weight loss • Skin hyperpigmentation • Serum cortisol level decreased • Abnormal ACTH stimulation test • Increased eosinophils

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Table 3
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Condition	What Is Common with FMS	What Is Different from FMS
Hypothyroidism[38]	• Fatigue • Cognitive difficulties • Cold intolerance • Constipation • Weight gain	• Hair loss texture change • Goiter • Dry skin • Bradycardia • Decreased deep tendon reflexes • Abnormal thyroid function tests

Abbreviation: ACTH, adrenocorticotropic hormone.

IS LABORATORY TESTING NECESSARY IN FIBROMYALGIA SYNDROME?

Patients with FMS have normal laboratory tests thus blood work is indicated to exclude other conditions that could have similar symptoms and should be limited to hemogram, basic metabolic panel, sedimentation rate, C-reactive protein, and thyroid-stimulating hormone.[40] Routine testing for rheumatoid arthritis or systemic lupus erythematosus is discouraged unless the patient has features to specifically suggest these conditions. In particular, testing for antinuclear antibodies (ANA) can be confusing for the patient because a positive ANA low titer is common in the general population.[41] In particular, ANA tests of low titer less than or equal to 1:160 were found to have a very low (9%) positive predictive value for any connective tissue disease.[42] "At present, ANA positivity occurs so commonly in patients with musculoskeletal complaints and vague symptomatology that a positive results might be neither revealing nor informative: indeed ANA positivity might muddle an otherwise sensible and parsimonious diagnosis work-up."[41]

EVALUATION AND TREATMENT OF THE PATIENT WITH FIBROMYALGIA SYNDROME

Patients diagnosed with FMS are a heterogenous group that require individualized management based on FMS severity and contributing factors.[43]

Education is an essential part of FMS management and should validate the symptoms, reassure, shift focus from symptom management to maintaining function, and emphasize self-pacing and self-management strategies.[44] Patients should be directed to identify their stressors and focus on those who can be eliminated. The University of Michigan Fibro Guide is a free interactive application that uses a cognitive behavioral method to inform and help patients self-manage FMS symptoms.[45] The first step in management should be a graded and stepwise approach prioritizing exercise, mindfulness, and psychological interventions such as cognitive behavioral therapy targeting pain. Finding mental health providers in the community with expertise in cognitive behavioral therapy and interest in FMS can be extremely helpful in managing FMS. Exercise, including aerobic, strengthening, combination of the 2, and mind and body exercises such a Tai chi empower patients to take control and were shown to reduce FMS severity and catastrophizing, improving affect and physical functioning.[46–49]

Patients who do not respond to nonpharmacological interventions may have maladaptive pain responses and/or suffer from sleep disorders and/or active psychiatric conditions (**Table 4**). These patients may require in-depth psychiatric and psychological care, sleep evaluation, and may benefit from added drug therapy.

Table 4
Evaluation and treatment of the patient with fibromyalgia syndrome

Domains	Evaluation	Questionnaires	Approach	Drugs Used in Patients with FMS
Mood	• Prior history of depression, anxiety, other psychiatric conditions • Seeing/seen psychiatry or psychology	• Depression (patient health questionnaire 9) • Anxiety (general anxiety disorder questionnaire) • Bipolar disorder (mood disorders questionnaire)	Mild to moderate: • Counseling • Psychology • Medications: SNRI should be chosen first, but other antidepressants can be tried if SNRI response inadequate or intolerant Severe: • Psychiatric consult	• SNRI • SSRI • Dopamine/norepinephrine reuptake inhibitor • Mood stabilizers
Sleep	• Unrefreshed sleep • Trouble falling and or staying a sleep • Prior history of primary sleep disorders (sleep apnea, narcolepsy, restless legs)		• Sleep hygiene education • Treatment of primary sleep disorders • Sleep medications	• Sleep supplements • Gabapentinoids • Tricyclic/tetracyclic antidepressants • Muscle relaxants
Physical deconditioning	• Moderate exercise at least 30 min 3 times a week		• Education about the role of exercise • Referral to physical therapy	
Stressful life events	• Past stressors: childhood and adulthood physical and sexual abuse, neglect, trauma, illness • Current stressors: financial, family, health, social		• Identify and try to eliminate reversible stressors • Psychological therapy for past trauma • Psychological interventions to change the stress response	
Maladaptive pain responses	• Rumination • Magnification • Helplessness	• Pain catastrophizing questionnaire	• Psychological interventions to address maladaptive pain response	

Many drugs are used to treat FMS, despite poor evidence for efficacy. The Food and Drug Administration (FDA) has approved a gabapentinoid (pregabalin) and 2 serotonin-norepinephrine reuptake inhibitors (SNRI) (duloxetine and milnacipran). Randomized double blind placebo controlled clinical trials in patients with FMS showed that only half of those taking any of these drugs experience a clinically significant (at least 30%) reduction in pain, and the number needed to treat to see a benefit varies between 8 and 14.[50] Similar observations have been made for gabapentin and various other SNRIs and serotonin reuptake inhibitors (SSRIs).[51] There may be subgroups of patients with FMS who benefit more from drug therapy; an SNRI or SSRI drug may be useful in a depressed patient with FMS, whereas a gabapentinoid, a muscle relaxant, or a tricyclic antidepressant at bedtime may be the first choice in those with disturbed sleep. An evaluation for sleep apnea may be helpful in patients with FMS, especially those who are obese. As a general principle if a drug fails to show benefit after 1 to 2 months it should be discontinued. Opioid drugs should not be prescribed for FMS pain.[44]

Patients with severe fibromyalgia such as those who suffer from severe depression, bipolar disorder, or other complex psychiatric conditions and those who catastrophize, take opioids, are refractory to exercise, or seek disability need a much more intensive multidisciplinary care that involves physical therapy, occupational therapy, psychiatry, and psychology.

CLINICS CARE POINTS

- Fibromyalgia is a rule in (not rule out) diagnosis: extensive testing is not required for diagnosis.
- Each patient with fibromyalgia should be evaluated with regard to: stressors, exercise, mood, catastrophizing/maladaptive pain responses, and sleep.
- The treatment of fibromyalgia should be individualized. "One size does not fit all."
- The current FDA approved treatments have limited benefit.
- Medications that are not found effective should be discontinued.
- Nonpharmacologic interventions such as education, exercise, occupational therapy, psychological interventions, and cognitive behavioral therapy should be prioritized.

DISCLOSURE

The author has nothing to disclose.

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