Head and Neck Manifestations of Fibromyalgia and Chronic Fatigue Syndrome

16

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Introduction

Fibromyalgia (FM) and chronic fatigue syndrome (CFS) are both classified as functional somatic syndromes and can be characterized by varying degrees of myofascial pain and fatigue in the absence of objective causes [1, 2]. FM primarily involves chronic multifocal pain often musculoskeletal in nature and occurs in 2–5% of the population [3], whereas CFS is characterized by extreme fatigue with a prevalence of 0.5–2.5% [4]. CFS also takes on the name of myalgic encephalitis (ME) due to the nature of clinical symptoms revolving around myalgia, fatigue, and cognitive difficulties [5].

Although considered separate entities, FM and CFS have many overlapping symptoms with pain and fatigue both present in each, as well as a myriad of other findings such as headaches, cognitive dysfunction, stiffness, tenderness, depression, and other chronic pain syndromes such as low back and jaw pain [6]. For this reason, diagnosis of the two syndromes can be difficult and may require close attention to clinical symptom characterization. Even so, patients may often have concomitant FM and CFS, with Abbi et al. revealing that 34% of patients with CFS also have FM [7]. Additionally, it is estimated that both FM and CFS demonstrate a markedly higher prevalence of two to six-fold in women over men [1, 5–7]. FM more often affects people aged 55–64, whereas CFS is most often seen in patients from 20 to 40 years of age [7, 8].

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There have been multiple proposed diagnostic criteria of FM by two different organizations, the American College of Rheumatology (ACR) and the Analgesic, Anesthetic, and Addiction Clinical Trial Translations Innovations Opportunities and Networks (ACTTION) in conjunction with the American Pain Society (APS). The first diagnostic criteria for FM were developed by the ACR in 1990, focusing on having widespread pain throughout one's entire body along with a minimum number of 11 of 18 pre-determined tender spots for at least 3 months of symptom duration [1]. However, many found the physical examination of tender spots to be impractical [9]. These initial diagnostic criteria also did not consider other symptoms such as fatigue and sleep difficulties. Subsequently, in 2010, the ACR proposed a new set of diagnostic criteria for FM, this time focusing on the use of two subjective symptom scales: the Widespread Pain Index (WPI) and the symptom severity scale (SSS) (Table 16.1) [9]. The WPI focused on characterizing areas of pain, with 19 areas being examined. The use of the WPI index shifted the focus from chronic widespread pain to multisite pain, or a count of the number of body sites with pain. The SSS tested for other clinical symptoms such as cognitive deficits, fatigue, muscle weakness, and waking up unrefreshed. These indices were then modified multiple times, with the latest proposed changes to the 2010 ACR FM

Table 16.1 Diagnostic Criteria for Fibromyalgia and Chronic Fatigue Syndrome

Fibromyalgia			Chronic Fatigue Syndrome by IOM
2010 ACR	2016 modification of 2010 ACR	AAPT criteria	
• WPI[a] >7 and SSS[b] >5 OR WPI 3–6 and SSS >9 • 3-month duration of symptoms • No other disorder to explain the plain	• Involvement of 4 of 5 body sites (left upper, right upper, left lower, right lower, axial) • WPI ≥7 and SSS ≥5 OR WPI 4–6 and SSS ≥9 • 3-month duration of symptoms	• Multisite pain including ≥6 of 9 sites (head, R/L arm, chest, abdomen, upper back and spine, lower back and spine, R/L leg) • Moderate to severe sleep problems OR fatigue • 3-month duration of symptoms	• The following three symptoms: – Impairment of ability to engage in occupational, educational, social, or personal activities accompanied by fatigue not alleviated with rest for at least 6 months – Post-exertional malaise – Unrefreshing sleep • And at least 1 of the following: – Cognitive impairment – Orthostatic intolerance

ACR American college of rheumatology, *AAPT* Analgesic, Anesthetic, and Addiction Clinical Trial Translations Innovations Opportunities and Networks –American Pain Society Pain Taxonomy, *IOM* Institute of Medicine, *L* left, *R* right, *SSS* symptom severity scale, *WPI* widespread pain index

[a]The WPI measure the number of painful body regions from a list of 19 areas (R/L jaw, neck, R/L shoulder girdle, R/L upper arm, R/L lower arm, chest, abdomen, upper back, lower back, R/L hip, R/L upper leg, R/L lower leg)

[b]The SSS measures the degree of fatigue, feeling unrefreshed after sleep, cognitive symptoms, and number of general somatic symptoms

diagnostic criteria occurring in 2016. The 2016 modifications added another criterion: pain must be present in at least four of five body regions (composed of four quadrants and the axial area) [10]. This was in order to reduce the misclassification of regional pain syndrome with FM [11].

In a similar vein, the ACTTION-APS working group formed the ACTTION-APS Pain Taxonomy (AAPT) to establish a set of diagnostic criteria apart from the ACR in order to establish a common taxonomy across all chronic pain syndromes (including FM) and also to increase ease of use and clarity of criteria in the clinical setting [12]. The APPT focused on using an evidence-based approach and listed core diagnostic criteria that included the use of multisite pain counts (≥6 from a total of 9 different sites), other clinical symptoms outside of pain (sleep problems or fatigue), and a total duration of at least 3 months (Table 16.1) [13]. In addition to this, the AAPT recognized FM to be a multifaceted and heterogeneous disease state, and defined other common features, medical co-morbidities, and psychosocial factors that may be related to FM, however not necessary for diagnosis. As no diagnostic criteria have been deemed the gold standard for FM, both the ACR and APPT criteria have been used in clinical practice.

Similar to FM, the diagnostic criteria of CFS have varied over time, with previous definitions including symptoms such as post-exertional malaise, impaired concentration or memory, unrefreshing sleep, chronic pharyngitis, tender lymphadenopathy, headaches, muscle pain, or arthritic symptoms [2]. The most recent diagnostic criteria established by the Institute of Medicine in 2015 require three main symptoms: fatigue not alleviated by rest for 6 months in duration, post-exertional malaise, and unrefreshing sleep, with at least one of the following: cognitive impairment or orthostatic intolerance [14]. Table 16.1 demonstrates an overview of the diagnostic criteria for FM and CFS.

Multiple hypotheses have postulated the etiology of CFS and FM and have attributed these disease states to central sensitization, potential genetic predisposition, immune dysregulation/chronic inflammation, post-viral sequelae, or environmental factors. Central sensitization, also known as an increased central neuronal responsiveness contributing to allodynia and hyperalgesia, has been long established as a theory regarding the chronic widespread pain seen in FM. The reason for this hyper-responsiveness may be due to the alterations in neuromodulatory compounds (e.g., substance P) or abnormalities of neurological structures fundamental to pain perception [15]. More recently, altered pain thresholds in patients with CFS may provide support for central sensitization to play a role in CFS as well [15].

A commonly considered etiology of CFS was that of viral origin. Specifically, it was previously thought that CFS arose in the setting of viral triggers such as Epstein-Barr virus (EBV), cytomegalovirus (CMV), and human herpesviruses (HHV) [16]. These viruses were thought to incite immune dysregulation even following the resolution of the viral illness itself, leading to a chronic viral infection that manifests itself in the form of CFS. In fact, viral-like illnesses may precede CFS infections in about 50–80% of cases [17]. Nevertheless, the direct viral causation of CFS has not been confirmed and remains an area of active investigation.

Whatever the etiology, many consider severity and management of FM/CFS in the context of a biopsychosocial model [2]. Specifically, it has been seen that lifestyle factors such as acute stress or lack of personal and/or professional life satisfaction can trigger flare-ups in patients with FM [1]. It is clear that both FM and CFS can be so functionally impairing that they make daily activities of living cumbersome, and a greater portion of patients with FM (31% vs. 2% in healthy controls) report some form of work disability attributed to their medical condition [18]. Likewise, patients with CFS have reported a 54% reduction in work productivity compared to those without [19].

Interestingly, in addition to the commonly associated symptoms of pain and fatigue, many patients with FM/CFS may also experience a number of otolaryngologic symptoms or co-morbidities, such as hearing loss, tinnitus, allergic rhinitis, functional voice disorders, chronic pharyngitis, as well as temporomandibular joint disorders (TMD) (see Fig. 16.1). As these symptoms are not a part of either diagnostic criteria for FM or CFS, many times they can be overlooked. Therefore, the association between FM/CFS and otolaryngologic symptoms is further characterized in this chapter to provide readers with a heightened awareness of the overlap of these conditions.

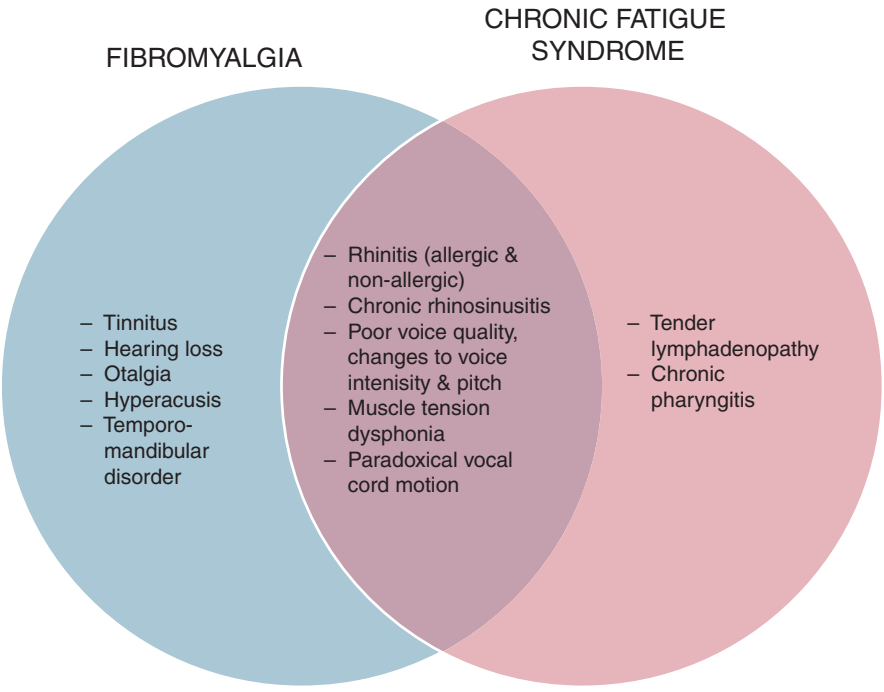

Fig. 16.1 Key otolaryngologic symptoms of fibromyalgia and chronic fatigue syndrome

Otology

FM has been associated with various otologic symptoms including hearing loss, tinnitus, otalgia, and hyperacusis. It has been hypothesized that changes in central sensitization and perception of sensory stimuli may explain the development of otologic findings after FM onset. To our knowledge, no research has found significant otologic symptoms associated with CFS, so the following section will be limited to a discussion of FM.

Many patients with FM report some degree of subjective, or self-reported, hearing loss following a diagnosis of FM. Bayazit et al. found that 12.5% of patients with FM who were enrolled in their study reported a subjective hearing loss on the Fibromyalgia Impact Questionnaire [20]. Similarly, Koca et al. shared that 45.4% of patients with FM reported "hearing problems," which was significantly higher than healthy volunteers (13.6%) [21]. Stranden et al. also reported that patients with FM are more likely to report subjective hearing loss [22]. Interestingly, they adjusted their measurement for audiometrically measured hearing loss; that is, the patients with FM reported subjective hearing loss more than the non-FM controls when matched for objective hearing threshold. However, while self-reported subjective hearing loss has a frequently reported association with fibromyalgia, the same cannot be said definitively for objectively measured hearing loss.

Objective hearing loss is commonly evaluated by electrophysiology studies, such as auditory brainstem measuring or otoacoustic emissions testing, and by audiometry, in which increases in hearing thresholds represent hearing loss. For the patients with FM who reported subjective hearing loss in Bayazit's study, no objective hearing loss was reported based on the pure-tone average and speech discrimination score components of audiometric analysis [20]. Interestingly, Koca's audiometry revealed a significant difference in hearing assessment findings between patients with FM and healthy volunteers, with patients with FM having higher hearing thresholds, and thus more hearing loss, across all frequencies (250 to 12,000 Hz) [21]. The type of hearing loss (sensorineural vs. conductive) was not specified. Notably, none of the patients in Koca's study had a history of hearing loss prior to audiometry performed during this study. Le et al. performed a large study in which patients with FM presented with a higher incidence of hearing loss than the control group [23]. Moreover, those with FM had a significantly higher risk for overall (1.46-fold), conductive (1.34-fold), sensorineural (1.46-fold), and mixed (1.56-fold) hearing loss. Patients with FM were found to have a higher risk of sensorineural hearing loss than conductive hearing loss, and among those with sensorineural hearing loss, bilateral sensory hearing loss was the most common. There is plenty of research conveying that FM patients more frequently report subjective hearing loss, but the connection between FM and objectively measured hearing loss is less clear and requires further study. Studies have not discussed treatment for hearing loss specifically in FM patients. However, hearing aids and other hearing rehabilitation devices are considered the mainstay of treatment for sensorineural hearing loss in general and should be considered in this population.

Subjective tinnitus is another otologic finding that has been associated with FM, with many patients experiencing tinnitus sometime after the onset of FM. Koca et al. shared that over half of their patients with FM (63.6%) had self-reported tinnitus when asked to select "yes" or "no" for the presence of the sensation [21]. Bayazit et al. similarly reported the presence of subjective tinnitus in their group of patients with FM (16.7%), which was a far lesser prevalence than other studies, but still more than the prevalence of tinnitus in the general American population (9.6%) [20, 24]. Iikuni et al. evaluated the time point at which patients experienced tinnitus, either before FM onset or after diagnosis of FM, and demonstrated that there was a significant increase in reported subjective tinnitus after FM onset [25]. Additionally, Cil et al. found that 74.3% of their patients with FM had self-reported tinnitus as identified using the Tinnitus Handicap Inventory (THI) [26]. This questionnaire was again administered after patients underwent a trial of pharmacologic treatment of either Pregabalin or Duloxetine. Interestingly, taking medication was found to significantly decrease subjective tinnitus as measured by the THI, but no significant difference was found between the treatment results of the two medications. These findings suggest that patients with FM may develop subjective tinnitus at a higher rate than the general population and that they may be amenable to pharmacologic treatments such as anti-convulsants, antidepressants, and muscle relaxants [27].

Otalgia has also been seen to manifest after FM onset. Iikuni et al. evaluated whether patients experienced chronic earache in one or both ears before FM onset as well as at the time of the study [25]. The team discovered a significant increase in reported otalgia in one or both ears after FM onset in this group. Likewise, Da Silva et al. reported that significantly more patients with FM complained of bilateral earache when compared with non-FM controls despite being on a treatment regimen for FM most commonly consisting of antidepressants, physical therapy, or opioids, at the time of the study [28]. It is unknown whether FM can cause otalgia. In patients presenting with otalgia, it is important to evaluate for all possible causes including malignancies of the skull base, pharynx, and larynx. Currently, we recommend that FM patients with otalgia that cannot be attributed to any other source be treated conservatively with analgesics at the discretion of the provider.

The development of hyperacusis is a less-discussed phenomenon that may occur in patients with FM and is defined by markedly decreased tolerance for sounds at ordinary intensities. Geisser et al. used two different methods to evaluate the presence of hyperacusis in their study population of patients with FM and healthy controls [29]. First, they administered a hyperacusis questionnaire, which asked participants to answer questions about what real-life sounds are bothersome and at what volume. The questionnaire was scored to convey the degree of hearing sensitivity. Geisser's group found that patients with FM experienced a significantly higher hearing sensitivity than controls [29]. The second test that the group administered obtained loudness discomfort levels for each ear separately and then

averaged the numbers to provide a single score. They found that patients with FM needed significantly lower auditory stimulation to report low, medium, and high pain intensity than healthy control subjects. Furthermore, Suhnan et al. conducted a literature review and concluded that FM patients may be more likely to develop hyperacusis as the disease progresses [30]. In terms of treatment, retraining and acoustic therapies traditionally used to alleviate hyperacusis may be worthwhile in this patient population with FM [31].

As previously mentioned, FM is a disorder in which there is an alteration in central sensitization leading to hyper-responsiveness to certain stimuli and pain signals. It is hypothesized that the otology symptoms associated with FM also stem from this phenomenon. Suhnan et al. examined global central sensitization in the context of hyperacusis and offered a few possible mechanistic explanations for this finding [30]. One idea they presented is that FM patients may experience a disturbance in pain-inhibitory mechanisms, leading to sensitization of both pain-specific and more general neurons in the spinal dorsal horn. They supported this claim by citing the weakened pain-inhibitory effect of noradrenaline in FM patients. The group concluded that otologic findings may be a result of the auditory system having connections to these very nociceptor centers in the brain due to a potential relationship between the processing of sound and bodily pressure-pain stimuli. Montoya et al. expounded on this idea by looking at pressure-pain thresholds in the hands and event-related brain potentials for patients with FM [32]. They found that these patients had abnormal processing of pain-related information as well as altered adaptation to pain stimuli. The group claimed that their findings could explain the presence of otologic symptoms in FM. Standen, Le, and Bayazit have independently offered their support in favor of this possible mechanism to explain the presence of hearing loss, tinnitus, and otalgia in patients [20, 22, 23]. Likewise, Iikuni et al. supported the idea that a central perceptual issue was behind these symptoms because they found no objective evidence of otologic changes [25]. A processing abnormality would also explain why only some patients experience these alterations.

Dizziness

Dizziness is a neuro-otological finding that may be seen in patients with FM and CFS. Koca et al. administered a Dizziness Handicap Inventory (DHI) to patients with FM to evaluate self-perceived handicapping effects of dizziness on quality of life, where a score is computed out of 100 with higher numbers representing the worse quality of life [21]. They found that the mean score was 24.6 for those with FM which was significantly higher than the control group's mean score of 11.7. Sawada et al. asked a group of patients with FM to complete a DHI and a version of the Fibromyalgia Impact Questionnaire (JFIQ) [33]. They found that

30.4% of the patients complained of dizziness, and the DHI and JFIQ scores were found to be correlated, meaning that the degree of subjective pain accompanying FM correlates with the degree of distress due to dizziness. It is hypothesized that the presence of dizziness in patients with FM can also be attributed to central sensitivity [21, 33]. Similarly, Collin et al. found that 58.2% of patients with CFS self-reported dizziness, and this information was used to sort patients into CFS phenotypes [34]. Garner et al. asked patients with CFS and healthy controls to use the Gracely Box Scale to self-rate their level of dizziness while recumbent and while standing [35]. They found that 38% of patients with CFS had recumbent dizziness and 72% of patients with CFS had standing dizziness, which was both significantly higher than healthy controls. Serotonergic medications, vestibular rehabilitation therapy, or psychotherapy may be considered for dizziness in patients with FM or CFS.

Rhinology

Both FM and CRS have been associated with a number of rhinological conditions, namely non-allergic rhinitis (NAR) and allergic rhinitis (AR) as well as chronic rhinosinusitis (CRS). In fact, the prevalence rate of FM in patients with rhinitis has ranged from 15–38% [36–38]. Additionally, when specifically examining patients with FM and/or CFS, rhinitis symptoms have been seen in 66–80% of patients [36, 39, 40]. Both positive and negative allergy skin tests resulted for these patients, making atopy a potential, however possibly not all-encompassing, a link between FM/CFS and rhinitis. In one study, nasal steroids were shown to be ineffective for the treatment of rhinitis in patients with CFS, with Kakumanu et al. revealing no significant differences in non-allergic rhinitis severity scores between use of nasal corticosteroids and saline spray as a placebo [41]. This might suggest patients with CFS may not respond to standard medical treatment for rhinitis [40]. Patients with both FM/CFS and rhinitis symptoms also appear to have a lower quality of life compared to those with rhinitis alone. Specifically, Gultana et al. demonstrated that a cohort of patients with concurrent FM and AR had significantly higher Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) and Nottingham Health Profile (NHP) scores, translating to poorer quality of life [37]. The largest differences in quality of life were seen in the following RQLQ domains: sleep, nasal problems, and emotions.

Numerous hypotheses have been investigated to explain the coexisting symptoms of NAR/AR and FM. Gultuna et al. proposed neurogenic inflammation to be a potential shared mechanism of AR and FM. It has been seen that a nasal allergen challenge, to simulate conditions of AR, results in releases of neuropeptides such as substance P and calcitonin gene-related peptides, which have also been under investigation in the pathogenesis of FM. Regarding another popular hypothesis that has been previously mentioned, many have attributed the common link between NAR/AR and FM, CFS, as well as other functional syndromes, to the role of central sensitization across these conditions.

Even more often than nasal congestion, patients with CFS may frequently experience symptoms of rhinosinusitis including facial pressure, frontal headache, and postnasal drip [40, 42]. The overall presence of sinus disease in patients with FM and CRS has not been well elucidated, however, Soler et al. did demonstrate a 9% prevalence of an FM diagnosis in a cohort of patients with medically refractory CRS versus 2–5% of FM in the general population [3, 43]. Fatigue is a commonly reported symptom in all patients with CRS [44]; Reh et al. reported that fatigue trumped congestion or nasal discharge as the most debilitating CRS symptom in 14% of patients with CRS as diagnosed by the clinical practice guidelines from the American Academy of Otolaryngology [45]. This demonstrates that fatigue may be an overlapping symptom in CRS and CFS.

In patients with CRS and FM who are refractory to medical management, surgical intervention may be appropriate. Improvement of quality of life and reduction of fatigue following endoscopic sinus surgery for CRS is comparable for patients with and without FM. Some may attribute this to result from relief of nasal obstruction, a decrease in inflammatory systemic mediators, or from a decrease in disease-associated emotional stress. Whatever the reason, Sautter et al. demonstrated that patients with FM and CRS had higher baseline fatigue visual analog scale (VAS) scores than patients with CRS alone and experienced a greater reduction of fatigue following surgery [44]. Soler et al. similarly found patients with both FM and CRS to have a poorer baseline quality of life compared to patients with CRS alone, as seen by the elevated rhinosinusitis disability index (RSDI) and chronic sinusitis survey (CSS) [43]. Patients with FM and CRS had comparable improvement in quality of life measurements as compared to patients with CRS alone following ESS. Altogether, symptoms of rhinitis and rhinosinusitis are prevalent in patients with FM and/or CFS, and can dramatically contribute to a poorer quality of life. Notwithstanding, management of rhinitis in patients with FM/CRS should follow routine treatment paradigms as those in non-FM/CRS patients.

Laryngology

Patients with FM or CFS have been seen to present with alterations to voice quality as well as a number of functional laryngological disorders. Gurbuzler et al. hypothesized that changes in voice intensity and pitch may be prevalent among patients with FM, as voice is dependent on both air expiration from the lungs as well as the vibrations from the oscillating vocal folds, and FM patients had been seen to have decreased respiratory muscle strength [46, 47]. In a cohort of 30 patients with FM, Gurbuzler et al. found significant subjective voice difference between patients with FM and the control group when comparing two administered scales: the grade, roughness, breathiness, asthenia and strain (GRBAS) scale and the Voice Handicap Index (VHI-10) [46]. The GRBAS scale is assessed by an external individual listening to and grading the quality of the patient's voice. The VHI-10 is a patient's

self-assessment of how changes in their voice have affected their daily life. Specifically, patients with FM had a significantly higher VHI-10 and GRBAS scores than patients in the control group, indicating impaired perceived voice quality. Additionally, patients with FM were also found to have a shorter maximum phonation time and a decrease in voice intensity.

Functional laryngological disorders have also been associated with patients with FM and CFS and can include muscle tension dysphonia (MTD) and paradoxical vocal fold motion disorder [48]. Prevalence of these laryngological disorders among patients with FM and CFS is not well known, however, it has been investigated by Piersiala et al. in an investigation of 215 patients with a chronic pain syndrome (CPS) (including patients with FM, CFS, or irritable bowel syndrome (IBS)) versus 4034 control patients [49]. Patients with CPS were more likely to have MTD and paradoxical vocal cord motion, and less likely to have laryngeal or airway pathology such as vocal fold lesions or anatomical airway alterations like glottic or tracheal stenosis. In fact, patients with a CPS had 1.8 increased odds of having muscle tension dysphonia and 2.5 increased odds of having paradoxical vocal fold motion over control patients. Although Piersiala et al. did not examine the FM and CFS patients separately from the IBS patients, these conclusions may still be pertinent in our discussion of FM and CFS. The results of Piersiala et al. propose two major considerations in that (1) the diagnosis of FM or CFS is a risk factor for MTD development and/or (2) that FM/CFS and MTD have similar underlying pathophysiology [48, 49]. In addition to this, the prevalence of FM and CFS was studied in patients with MTD, with Craig et al. examining a group of 153 patients with MTD. It was noted that 30% had other comorbidities, including 8% with FM and 1.3% with CFS [50].

Overall, patients with FM and CFS may present with poorer voice quality and experience concomitant functional laryngological disorders such as MTD and paradoxical vocal fold motion. Notwithstanding, the degree of disorder and treatment efficacy in our patient population of interest may require further investigation.

Temporomandibular Disorders

Temporomandibular disorders (TMD), defined as any symptoms or signs associated with the temporomandibular joint, have been found to often accompany FM. Truta et al. highlighted a phenomenon referred to as masticatory FM, in which patients experience pain while using their chewing muscles, as well as tenderness to palpation in the setting of normal radiographic imaging [51]. Truta et al. also recommended that this variation of FM be treated first with antispasmodics with central analgesic properties, followed by orthotics or physical, behavioral, or pharmacologic treatment based on response. In a review of 19 studies, Ayouni et al. found a strong association between TMD and FM, demonstrating that patients with FM had around an 80% prevalence of

TMD signs/symptoms such as temporomandibular joint pain, along with tenderness to palpation along muscles of mastication [28, 52–54]. TMD prevalence was also found to be significantly higher in FM (53%) than in failed back syndrome (11%), the latter of which served as a chronic pain control group [55]. Moreover, Leblebici et al. reported that 52% of patients with TMD also had FM, and Velly et al. reported that the presence of FM predicted the persistence of clinically significant TMJ pain after 18 months, without prescribed treatment (OR 2.48, $p = 0.02$) [54, 56]. It was also concluded that in patients with FM, the pressure-pain threshold in bilateral trigeminal areas was lower than in healthy controls. The authors commented on these findings by similarly suggesting that alterations in central processing mechanisms could serve as an explanation. It is important to be aware that patients with FM may develop TMD, and vice versa.

Chronic Pharyngitis (Table 16.2)

CFS is thought to occasionally present with chronic pharyngitis or a seronegative EBV-like presentation. In fact, chronic pharyngitis as a symptom has been a previous diagnostic criterion of CFS (2). Collin et al. organized a group of CFS patients into 6 symptom-based phenotypes, of which one was sore throat/painful lymph nodes, and found that only 4.5% of the patient population was categorized as this phenotype [34]. Similarly, other studies, such as Hickie et al., have also used sore throat as part of their inclusion criteria in CFS patients, and Sullivan et al. further reported that 12% of self-reported fatigued patients without formal CFS diagnosis complained of sore throat [57, 58]. Patients with CFS of the sore throat phenotype comprised a very small percentage of all CFS patients and additionally had markedly lower fatigue scores and higher physical function scores than other patients with CFS, demonstrating that chronic pharyngitis is prevalent, but not pervasive in all patients with CFS [34, 58].

Conclusions

This chapter has outlined specific otolaryngologic symptoms that have been observed in FM and CFS. The notable prevalence of these symptoms suggests that clinicians should not only monitor patients with FM and/or CFS for the development of head and neck symptoms but also should increase their diagnostic index of suspicion for FM and CFS in healthy patients who have a new development of these symptoms. Future directions should focus on revealing the mechanisms responsible for the otolaryngologic findings in these two functional disorders. Investigation of these pathophysiologic pathways will allow for the development of targeted management or treatment regimes.

Table 16.2 Overview of literature regarding FM/CFS and ENT-related clinical symptoms

Study (year)	ENT-related disease	Design	Population (n)	Outcome	Conclusions
Gurbuzler (2013)	Dysphonia	Prospective cohort	FM (31) versus controls (31)	Grade, roughness, breathiness, asthenia, and strain (GRBAS) voice scale; VHI-10; laryngostroboscopy, acoustic analysis, maximum phonation time	Patients with FM had poorer perceived voice quality over controls, with a VHI-10 score of 7.9 vs. 1.3 ($p < 0.001$) and a GRBAS scale of 2.5 vs. 0.6 ($p < 0.001$).
Piersiala (2020)	Muscle tension dysphonia, paradoxical vocal cord paralysis	Retrospective cohort	Patients with a CPS (215) versus controls (4034)	Prevalence and odds ratios of different voice and functional voice disorders, laryngeal pathology, and airway/swallowing problems	Patients with CPS were more likely to present with muscle tension dysphonia (OR 1.9, 95% CI) or paradoxical vocal cord paralysis (OR 2.5, 95% CI) and less likely to present with laryngeal pathology (OR 0.77, 95% CI) or airway problems (OR 0.47, 95% CI)
Craig (2015)	Laryngology	Retrospective cohort	Patients with muscle tension dysphonia (153)	Changes in VHI scores following differing treatment options (voice therapy alone or with physical therapy, physical therapy alone, no treatment); prevalence of comorbidities including FM and CFS.	30% of patients with MTD had a comorbid condition including 8% with FM and 1.3% with CFS. Presence of comorbidities had no effect on baseline VHI scores or VHI improvement following treatment.
Gultana (2019)	Rhinitis	Retrospective cohort	Patients with AR (105)	Prevalence of FM and impact on quality of life using RQLQ and NHP scores	Prevalence rate of FM in patients with AR was 32%. Patients with both FM and AR have decreased RQLQ and NHP scores.
Tsiakiris (2017)	Rhinitis	Retrospective cohort	Patients with AR (298), allergic asthma (164) versus controls (2876)	Prevalence of functional somatic syndromes (FM, irritable bowel syndrome, migraine) expressed using OR	Prevalence rate of FM in patients with AR was 15%. Patients with AR had an adjusted OR of 3.5 (95% CI 2.0–6.4) over controls of having FM.

Cleveland (1992)	Rhinitis	Prospective cohort	Patients with rhinitis (allergic and non-allergic) (48)	Prevalence of symptoms of rhinitis including congestion, rhinorrhea, postnasal drip. Prevalence of FM per 1990 ACR criteria.	Prevalence rate of FM in patients with rhinitis was 38%.
Michaud (2006)	Sinus-related symptoms	Retrospective cohort	Patients with rheumatic arthritis (7243), osteoarthritis (1667), and FM (447)	Rate of physician visits for sinus problems in last 6 months from time of study, lifetime and rates of over the counter and prescription sinus medications	Prevalence rate of sinus problems in patients with FM in the last 6 months or at any time point was 25% and 63%, respectively. Of patients with FM, 37% and 35% used OTC or prescription sinus medication respectively.
Sautter (2008)	CRS	Prospective cohort	Patients with CRS (272)	Changes in fatigue following endoscopic sinus surgery evaluated using a 10-point VAS	Prevalence rate of FM in patients with CRS was 5%. Following ESS, patients with CRS and FM showed greater reductions in fatigue than patients with CRS alone.
Soler (2008)	CRS	Prospective cohort, case–control analysis	Patients with CRS (283)	Changes in QOL scores following endoscopic sinus surgery including the RSDI and CSS	Prevalence rate of FM in patients with CRS was 9%. Following ESS, patients with CRS with FM showed comparable rates of improvement in QOL compared to patients with CRS without FM.
Bayazit (2002)	Hearing loss, tinnitus	Prospective cross-sectional	Patients with FM (25)	Subjective hearing loss using FM impact questionnaire; subjective tinnitus using patient's history and standard otolaryngologic examination including audiologic assessment.	12.5% of FM patients reported subjective hearing loss with normal objective otolaryngologic examinations. 16.7% of FM patients reported subjective tinnitus.
Koca (2018)	Hearing loss, tinnitus	Prospective cross-sectional	Patients with FM (45) versus controls (45)	Subjective hearing problems and tinnitus using questionnaire; audiogram and tympanogram for objective hearing loss.	Self-reported hearing problems ($P < 0.001$) and tinnitus ($P < 0.001$) were significantly higher in FM group than controls. Significant difference found between two groups in audiometry at frequencies 250–12,000 Hz.

(continued)

Table 16.2 (continued)

Study (year)	ENT-related disease	Design	Population (n)	Outcome	Conclusions
Le (2020)	Hearing loss	Retrospective cohort	Patients with FM (55169) versus controls (110338)	Prevalence of general and hearing loss subtypes	FM group had a higher incidence of hearing loss than the control group (4.03 vs. 2.33 per 1000 person-years). FM patients had 1.46-fold higher risk for hearing loss. Diabetes, hypertension, and Meniere's disease increase risk of objective hearing loss in FM patients.
Standen (2016)	Hearing loss	Retrospective cross-sectional	Patients with subjective hearing loss (44494)	Prevalence of FM.	Prevalence of FM in patients with hearing loss was 3.3%. Those with FM had increased probability of reporting subjective hearing loss compared to non-FM controls matched for objective hearing loss level (OR 5.2 for women and 4.4 for men).
Cil (2020)	Tinnitus	Randomized control trial	Patients with FM (101)	Prevalence of self-reported tinnitus; subjective level of tinnitus before and after treatment with pregabalin or duloxetine using tinnitus handicap inventory.	Prevalence of tinnitus was 74% in patients with FM. Tinnitus level after treatment was significantly lower than before ($P < 0.001$). No significant difference between pregabalin and duloxetine in a change in tinnitus level.
Iikuni (2013)	Tinnitus, otalgia	Retrospective cohort	Patients with FM (21)	Prevalence of recalled and self-reported tinnitus and otalgia before and after FM onset.	Prevalence of tinnitus and otalgia in patients with FM was 78% and 40%, respectively. Significant post-FM increase in tinnitus and otalgia ($P < 0.001$; $P < 0.001$).
Da Silva (2012)	Otalgia	Prospective cross-sectional	Patients with FM (26) versus controls (26).	Evaluation of orofacial pain.	Significantly more patients with FM reported earache compared to controls ($P = 0.038$).
Geisser (2008)	Hyperacusis	Prospective cross-sectional	Patients with FM (31) versus controls (29)	Prevalence and level of hyperacusis based on hyperacusis questionnaire.	Patients with FM experienced higher hearing sensitivity than controls and required significantly lower auditory stimulation to report a level of pain intensity.

Suhnan (2017)	Hyperacusis, central sensitization	Literature review	Patients with hyperacusis (10 papers)	Prevalence of hyperacusis in FM patients; pathophysiology of hyperacusis.	Patients with FM more likely to develop hyperacusis as disease progresses. FM patients may experience disturbance in pain-inhibitory mechanisms, leading to otologic findings.
Montoya (2005)	Central sensitization	Prospective cross-sectional	Patients with FM (12) versus controls (12)	Pressure-pain thresholds and event-related brain potentials in FM patients.	Patients with FM had abnormal pain processing and abnormal adaptation to pain stimuli compared to controls, which could lead to otologic findings.
Ayouni (2019)	TMD	Systemic review	Patients with FM and TMD (19 papers)	Prevalence of TMD in patients with FM.	Patients with FM have high prevalence of TMD or orofacial involvement. For these patients, pressure-pain threshold in trigeminal areas was lower than controls.
Collin (2016)	Sore throat	Prospective cross-sectional	Patients with CFS (8433)	Prevalence of symptom-based sore throat/painful lymph node phenotype of CFS.	4.5% of CFS patients presented with a sore throat/painful lymph node phenotype.

AR Allergic rhinitis, *CFS* chronic fatigue syndrome, *CPS* chronic pain syndromes, *CRS* chronic rhinosinusitis, *CSS* chronic sinusitis survey, *FM* fibromyalgia, *NHP* Nottingham health profile, *ENT* otolaryngology, *RQLQ* rhinoconjunctivitis quality of life questionnaires, *RSDI* rhinosinusitis disability index, *VHI* voice handicap index, *TMD* temporomandibular disorder, *QOL* quality of life

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