Sex-Specific Differences in Patients with Temporomandibular Disorders

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Aims: *To explore potential differences in characteristics of patients that might account for sex-specific differences in temporomandibular disorders (TMD).* ***Methods:*** *A total of 502 patients presenting with TMD during 2000 to 2002 at the Outpatient Unit for Functional Disorders of the Medical University of Vienna underwent detailed evaluation of their medical history and assessment of clinical findings. The data obtained were assessed for sex-specific differences by analysis of variance and multiple regression.* ***Results:*** *Overall, 404 females (mean age ± SD: 40 ± 16 years; range 12 to 96 years) and 98 males (mean age 41 ± 16 years; range 16 to 78 years) were included. Their rating of their pain on a visual analog scale (VAS) showed a significantly higher pain intensity for females than for males (*P = *.004). Clinical assessment showed a significantly lower degree of mouth opening for females than for males (*P < *.001). While no sex-specific differences were noted for clicking phenomena of the temporomandibular joint (TMJ) and for the bite class of the patients, bite anomalies were significantly more frequent in male patients (*P = *.03). Palpation of masticatory muscles and the TMJ revealed significantly higher tenderness on palpation in female as compared to male patients (*P = *.001). Grouping by clicking, crepitation, and bruxism also showed greater pain (VAS) and more tenderness on palpation in females versus males. Females also showed peaks of prevalence of TMD in the age group below 25 years and in the group 55 to 60 years, whereas males had a more even age distribution. No external factors, such as exposure to stress, were found that moderated the sex difference.* ***Conclusion:*** *Female TMD patients showed greater pain and muscle tenderness on palpation as compared to male TMD patients. They also showed a different age distribution of prevalence of TMD. These results were independent of subjective symptoms, clinical findings, and external factors.* J OROFAC PAIN 2013;27:42–50. doi: 10.11607/jop.970

Key words: gender differences, muscle tenderness on palpation, orofacial pain, sex differences, temporomandibular disorders

Various factors may induce or aggravate temporomandibular disorders (TMD). Such factors may include occlusal interferences,[1] hyperactivity of the temporal and masseter muscles,[2] bruxism,[3] and stress,[4] although it has not yet been clarified which of the factors play the primary role. Also, the frequency of cervical and neck problems[5] and posture anomalies[6] is higher in patients with TMD, and patients with cervical and neck problems also show an increased incidence of TMD symptoms.[7]

Various explanations have been suggested for the dominance of the female sex among TMD patients.[8–10] Some authors have indicated an age-related peak for TMD in the median third of female

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life.[11,12] This has been explained by hormonal changes.[11–14] In contrast, other investigations have reported the highest prevalence of TMD during the reproductive years,[15] beginning with puberty and decreasing after menopause.[11,16–18] Regarding the individual course of pain severity, a perimenstrual and periovulational peak of pain is common.[19] On average, female but also male TMD patients show higher serum estradiol levels than healthy subjects.[20]

Other attempts for an explanation have suggested sex-related differences in musculature. A higher share of the cross-sectional area of skeletal muscles of type IIa fibers has been found in male rats, while female animals showed greater cross-sectional areas of type I fibers.[21] Studies in healthy humans also showed larger muscle fibers[22] and a greater area of type II fibers in males and of type I fibers in females.[23,24] The smaller cross-sectional muscle area and higher frequency of type I fibers could lead to a higher prevalence of muscle tenderness in female patients.

Women show more pronounced pain responses to experimental noxious stimuli than men.[25–29] Female sex appears to be a risk factor for migraine[30,31] and for the chronification of back pain.[32] Among chronic pain patients, females more frequently show high pain intensity, require an increased number of treatment attempts, and use alternative therapies more frequently than males.[33] In addition, responses of females to analgesic therapy have been suggested to differ from those of males,[34] and women show differences in activation of the endogenous analgesia system in the central nervous system (CNS).[35]

Stress is closely interlinked with the development of dysfunctional syndromes. TMD patients show an enhanced response to stress stimuli compared to healthy subjects.[36] They suffer more frequently from distress, anxiety, or depression and show a reduced repertoire of coping strategies,[37] with catastrophizing and anxiety being associated with the severity of clinical TMD symptoms.[38,39]

The present study was therefore initiated with the aim of exploring potential differences in characteristics of patients that might account for sex-specific differences in TMD. The study was intended to relate medical history data and clinical findings in females and males for the purpose of testing the following hypotheses:

- When presenting with similar clinical findings, women with TMD show a higher pain perception and more tenderness on palpation than men with TMD.
- With respect to the severity of complaints, stress plays a greater role in women with TMD than in men with TMD.
- Males differ from females in their age-related prevalence of TMD.

Although an overall higher prevalence of TMD in women has been reported in several studies, the assumption that the difference between males and females is age-related has never, to the authors' knowledge, been addressed before.

Materials and Methods

The investigation was planned as a retrospective cross-sectional study of patients' histories and clinical examinations during a period with standardized procedures. The study was approved by the Ethics Committee of the Medical University of Vienna. Informed consent was obtained from all subjects.

The investigation included 502 consecutive patients presenting at the University's Outpatient Unit for Functional Disorders from 01/2000 to 12/2002 and undergoing detailed evaluation of medical history and clinical findings. All patients seeking medical advice and diagnosis of their disorders of the temporomandibular system underwent an initial interview. These patients were mostly referral patients; however, all were untreated except for occasional prescriptions of analgesics. Medication was predominantly for concomitant diseases and was considered in evaluating whether or not the symptoms were due to TMD. If symptoms were considered to be due to TMD, patients underwent a detailed standardized diagnostic evaluation and were included in the study. Patients suspected with other types of dysfunction were excluded from the study.

In the initial examinations the following data were obtained: patient's primary concern, general medical history (cardiovascular, respiratory, digestive problems; CNS and mental status; hormonal, rheumatic, and metabolic disorders; allergies) and dental evaluation (dental sensitivity, articular noises, pain in the temporomandibular joints [TMJs] and masticatory muscles at rest and in function, biting problems, neck tension, headache, tinnitus, and dry or burning mouth sensation). For these symptoms, the severity of the problem and the impairment of the capacity to work were classified in three categories: 1 = minor impairment (symptoms perceived only under specific conditions, no restriction of working capacity); 2 = moderate impairment (permanent awareness of the symptom but no restriction of working capacity); 3 = severe impairment (restriction of working capacity). In addition, previous accidents/injuries, surgery history,

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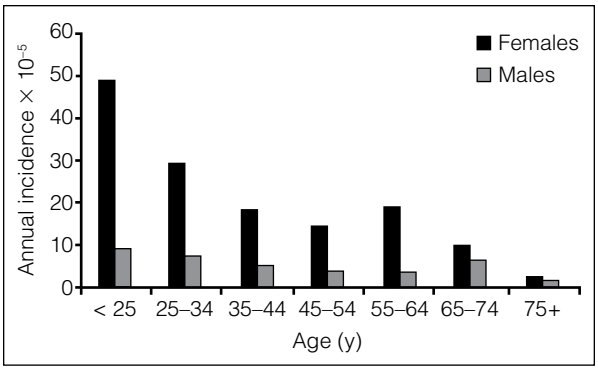

Fig 1 Estimates of annual incidences of TMD by age in males and females, assuming all patients in Vienna with TMD are presenting at the Outpatient Unit.

orthodontic and/or prosthetic treatment or splint therapies, existing problems with other joints, diurnal or nocturnal clenching and/or crepitation, nail biting, subjective description of personality (cheerful, sad, controlled, uncontrolled, short-tempered, calm), self-assessment of stress (family problems and/or job-related stress: yes/no), type of profession/occupation (whether it involves standing, sitting, speaking), and sleeping position (back, side, stomach) were evaluated. Temporomandibular pain (average pain of the last few weeks and maximal pain during that period) was scored by the patients on a visual analog scale (VAS) presented as a color scale with different shades of red and ranging from "no pain at all" to "most severe pain imaginable." On the backside of the scale, each color shade was assigned a value between 0 and 100.

A clinical examination was carried out by experienced experts following a standardized diagnostic procedure established at the Viennese dental clinic that is similar to the Research Diagnostic Criteria for TMD (RDC/TMD). Mouth opening in millimeters, bite class (left/right), presence of clicking phenomena (clicking yes/no, crepitation yes/no) and tenderness on pressure of joints and muscles (shoulder and neck muscles, atlanto-occipital joints, supra- and infrahyoid muscles, sternocleidomastoid muscles, temporalis muscles, masseter muscles, lateral and medial pterygoid muscles, mylohyoid and digastric muscles, TMJ lateral poles and retral joint spaces) were evaluated. The muscles on both sides were simultaneously palpated by hand. The mylohyoid muscle, the digastric muscle, and the medial pterygoid muscle were palpated consecutively; 900 g of extraoral and 500 g of intraoral palpation pressure was applied. Pressure calibration of the examiners was performed with a digital scale. No tenderness on pressure was graded with 0; the intensity of pain was scored separately for right and left side in a scale ranging from 1 to 3: 1 = perceivable difference in tenderness between the two sides, 2 = mild pain, 3 = severe pain.

Statistical Analyses

Statistical evaluation was performed by applying analysis of variance (ANOVA) with sex as the main factor. Secondary variables included bruxism (yes/no), stress (yes/no), suffering (below/above median), etc. For mouth opening, a sex-specific cutoff was defined as the mean minus one standard deviation (SD) in accordance with the study of Sawair et al.[40] In addition to sex as a main factor, interactions between sex and the secondary variables were investigated. Homogeneity of variance was tested by Levene's tests and normality by Lilliefors-corrected Kolmogorov-Smirnov tests. For all analyses, two-sided *P* values below .05 were considered significant. Due to the exploratory nature of analyses of the different variables except sex, no correction for multiple endpoints was performed. However, multiple regression analyses of pain (VAS) and muscle palpation results (muscle pain score) also were conducted and included all potentially explanatory symptoms and attributes as well as interaction terms.

Because of the large difference in the number of males and females, a minimum effect size that could be detected was computed based on the observed sample sizes (two-sided level of significance of 5% and a power of 90%). Under specified conditions, the detectable effect size "d" can be as small as .365.

Estimates of incidences were based on the total Viennese population averaged over the years of recruitment, assuming all patients fulfilling the inclusion criteria in Vienna were treated at the Outpatient Unit.

Results

The group evaluated included 404 females and 98 males. The average age of females was (mean ± SD) 40 ± 16 years (range, 12 to 96 years) and that of the males was 41 ± 16 years (range, 16 to 78 years). Age distribution showed a peak below the age of 25 years in the female group followed by a decrease and a second peak at the age of 55 to 64 years, while men showed a decreasing age distribution with a small increase at the age of 65 to 74 years (Fig 1).

Sex Differences

There was a trend for sex differences in primary concern ($P = .07$); 46% of females and 41% of males

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described pain as the primary concern, while clicking was the primary concern in 35% of males and 27% of females, bruxism in 9% of males and 5% of females, and problems with bite predominated in 3% of males and 2% of females.

General medical history revealed no significant differences except for hormonal problems that were more common in females (P = .03). There were no differences in dental clinical history between sexes. All findings evaluated in the dental clinical history were summarized in a score with regard to severity, which represented the subjective "degree of suffering." Sensitivity of teeth was described by 30% of patients (males and females), and problems with mouth closing, chewing, swallowing, or speaking by 10% of males and 15% of females. Articular noises were reported by 77% of male and 80% of female patients, and pain in the TMJ/auricular region by 74% of male and 71% of female patients. Headache and/or migraine was described by 40% of males and 35% of females, tinnitus by 8% of males and 11% of females, and a combination of headache/tinnitus was reported in 10% of males and 8% of females.

Concerning the specific medical history, significantly (P = .007) more males (41%) than females (29%) reported nocturnal bruxism, while no sex differences were seen for clenching and nail biting. Females showed a trend towards a higher rate of prosthetic restorations (P = .098). Males presented with a significantly higher frequency (P = .023) of a sitting profession/occupation. No differences between females and males were seen for accidents/injuries, surgery, existing problems with other joints, previous orthodontic or splint therapy, and sleeping position.

When asked for a description of their personality, significantly more females described themselves as cheerful (P = .03), while more males classified themselves as sad (P = .08) or short-tempered (P = .09). In addition, more males reported to suffer under (predominantly job-related) stress (P = .015).

Clinical examination showed a significantly smaller mouth opening for females than for males (P < .001); after correction for the difference in healthy males and females, the difference remained significant (P = .039). While clicking phenomena of the TMJ and bite class did not reveal any sex-specific differences, male patients presented with a significantly higher frequency of bite anomalies (P = .03).

Sex as a Mediator of the Relationship Between Clinical Factors and Pain

In the rating of pain on a VAS at the first appointment, females showed a significantly higher pain level than males (P = .004) (Fig 2). Even when the data were grouped according to the subjective degree of suffering, both the group below and that above the median level showed increased pain in the females as compared to the males. This finding remained unchanged when patients were grouped into those with and without clicking or those with and without crepitation noises. When the patients were grouped by mouth opening, muscle tenderness on pressure or bruxism also showed a higher level of pain for the females (Table 1).

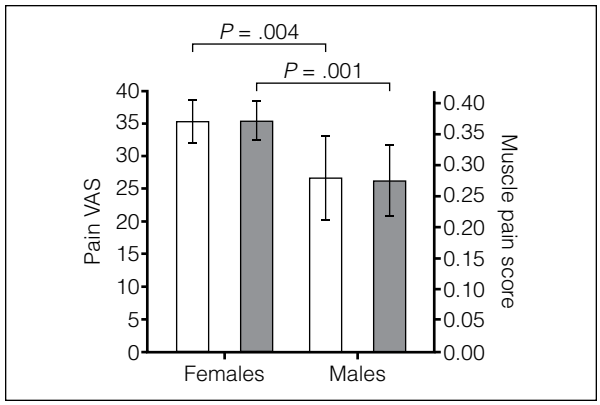

Fig 2 Mean values (with 95% confidence intervals) of pain intensity (VAS, white, left axis) and muscle pain scores (gray, right axis) for females and males.

Palpation of masticatory muscles and TMJs showed significantly more pain/tenderness on pressure for female than for male patients (P = .001) (Fig 2). When the data were grouped according to the subjective degree of suffering, the group of patients suffering below the median level showed only a slightly increased tenderness on pressure for females, while those with a subjective degree of suffering above the median level showed a distinctly higher tenderness on pressure for the females than for the males. When the patients were grouped by clicking noises, crepitation and bruxism also showed increased pain on palpation for the females versus the males (Table 2).

Multiple regression analyses supported the results obtained by ANOVA. Only sex was a significant predictor of both overall pain score (VAS) and muscle palpation results (Table 3). No moderating effect was found for any of the symptoms and attributes included. In the analysis of overall pain scores, muscle pain was also a significant predictor but independent of sex. Interestingly, a tendency for an interaction of sex with the suffering score was obtained, possibly indicating a specific difference with males showing less muscle pain on palpation at the same level of orofacial pain assessed by VAS.

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Table 1 Results of Two-Way ANOVA of Pain Score (VAS) with *P* Values for the Main Factors of Sex and Symptom (ie, the symptom stated in the first column) and Their Interaction*

	Females		Males		*P* value		
Symptom	%	X ± SE	%	X ± SE	Sex	Symptom	Interaction
Bruxism							
No	70.8	36.7 ± 2.0	59.2	29.4 ± 4.2	.033	.146	.794
Yes	29.2	32.0 ± 3.1	40.8	22.6 ± 5.1			
Crepitation							
No	82.7	33.8 ± 1.9	83.7	26.3 ± 3.6	.030	.281	.481
Yes	17.3	42.9 ± 4.0	16.3	28.2 ± 7.6			
Clicking							
No	29.2	37.8 ± 3.3	26.5	28.0 ± 7.2	.036	.534	.863
Yes	70.8	34.4 ± 2.0	73.5	26.1 ± 3.6			
Stress							
No	46.5	35.9 ± 2.5	31.6	28.1 ± 5.4	.039	.694	.873
Yes	53.5	34.9 ± 2.3	68.4	25.9 ± 4.1			
Suffering							
< Md	45.0	34.2 ± 2.5	41.8	21.2 ± 4.3	.015	.142	.356
≥ Md	55.0	36.3 ± 2.3	58.2	30.5 ± 4.6			
Mouth opening							
> Crit	69.2	34.8 ± 2.2	81.3	32.0 ± 4.1	.124	.824	.487
≤ Crit	30.8	39.6 ± 3.3	18.8	29.5 ± 8.8			
Muscle tenderness							
< Md	46.5	29.1 ± 2.4	62.2	21.5 ± 3.8	.082	.001	.824
≥ Md	53.5	40.8 ± 2.3	37.8	35.0 ± 5.8			

*A significant interaction would be obtained if the symptom has a differential effect depending on sex.
X, arithmetic mean; SE, standard error; Md, median; Crit-sex-specific cutoff, males (n = 98), females (n = 404).

Table 2 Results of Two-Way ANOVA of Muscle Palpation Score with *P* Values for the Main Factors of Sex and Symptom (ie, the symptom stated in the first column) and Their Interaction*

	Females		Males		*P* value		
Symptom	%	X ± SE	%	X ± SE	Sex	Symptom	Interaction
Bruxism							
No	70.8	0.36 ± 0.02	59.2	0.24 ± 0.03	.011	.081	.423
Yes	29.2	0.40 ± 0.03	40.8	0.33 ± 0.05			
Crepitation							
No	82.7	0.37 ± 0.02	83.7	0.28 ± 0.03	.030	.744	.768
Yes	17.3	0.40 ± 0.04	16.3	0.28 ± 0.06			
Clicking							
No	29.2	0.36 ± 0.03	26.5	0.23 ± 0.06	.007	.368	.505
Yes	70.8	0.37 ± 0.02	73.5	0.29 ± 0.03			
Stress							
No	46.5	0.37 ± 0.02	31.6	0.23 ± 0.04	.004	.289	.394
Yes	53.5	0.38 ± 0.02	68.4	0.30 ± 0.04			
Suffering							
< Md	45.0	0.35 ± 0.02	41.8	0.32 ± 0.05	.017	.570	.089
≥ Md	55.0	0.39 ± 0.02	58.2	0.24 ± 0.03			
Mouth opening							
> Crit	69.2	0.40 ± 0.02	81.3	0.33 ± 0.04	.049	.153	.464
≤ Crit	30.8	0.36 ± 0.03	18.8	0.22 ± 0.05			

*A significant interaction would be obtained if the symptom has a differential effect depending on sex.
X, arithmetic mean; SE, standard error; Md, median; Crit-sex-specific cutoff, males (n = 98), females (n = 404).

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Table 3 Results of Multiple Regression Analysis of Pain (VAS) and Muscle Palpation (Muscle Pain) on Sex, Age, Different Symptoms, and Interaction Between Symptoms and Sex

	Pain (VAS)		Muscle pain	
Variable	Standard coefficient	*P* value	Standard coefficient	*P* value
Sex	.246	.025	.154	.002
Age	.076	.093	.074	.110
Bruxism	–.097	.319	.142	.159
Crepitation	.008	.938	–.037	.738
Clicking	–.060	.563	.123	.252
Stress	–.039	.719	.109	.339
Suffering	–.038	.686	–.095	.328
Mouth opening	.012	.927	–.063	.643
Muscle pain	.254	.025	–	–
Bruxism × Sex	.021	.827	–.077	.437
Crepitation × Sex	.077	.467	.060	.585
Clicking × Sex	–.004	.971	–.098	.366
Stress × Sex	.018	.868	–.089	.425
Suffering × Sex	.066	.481	.165	.087
Mouth opening × Sex	.076	.558	.041	.759
Muscle pain × Sex	.017	.878	–	–

No sex-specific differences in the treatment prescribed were noted for splints and other therapies; however, significantly more females than males received physiotherapy ($P = .02$).

Discussion

The study showed significantly higher pain levels among female TMD patients. Sex-specific differences were seen for both subjective indicators such as pain sensation as well as for muscle tenderness on pressure. No differences were seen between females and males in articular noises. Since noises in the TMJ represent the result of morphologic articular changes, no differences are to be expected in this respect. Professional/occupational stress was more frequent in males but had no moderating effect on pain intensity or muscle tenderness; however, patients in this study were directly asked for their subjective stress load and no specific stress questionnaires were used. The presence of stress represented a risk factor for increased pain levels regardless of sex. This correlates with the findings of several other authors describing an association between stress, parafunction, and muscular pain.[41,42] No difference between males and females was observed for this correlation between stress and TMD symptoms, although females showed higher stress levels[43] and different cerebral responses to stress.[44] Women show a more sensitive response to stress-inducing events.[35] Females also differ from males in their response to stress; while females respond by increased cardiac output, males tend to respond by increased vascular resistance.[45]

Age distribution showed a peak below the age of 25 years in the female group followed by a decrease and a second peak at the age of 55 to 64 years, while men showed a decreasing age distribution with a small increase at the age 65 to 74. These findings are comparable with the results of Martins-Júnior et al,[46] who found a peak prevalence in the age range 20 to 30 years, and with Sener and Akgunlu,[47] who observed a higher prevalence at age 15 to 30 years compared with 30 to 45 years, although the correlation between sex and age was not investigated in this study. Other studies have reported a decrease in the TMD symptoms with increasing age,[48,49] but differences in these trends between males and females have not been investigated. A possible explanation for the observed age pattern is hormonal differences; various human and animal studies[11–20,50–53] have been conducted to find possible causes for the higher risk of women of child-bearing age to develop TMD.

The significantly smaller mouth opening found for females than for males in the clinical examination is in concordance with other studies, in which a smaller mouth opening of healthy women and

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TMD patients in comparison to healthy men has been demonstrated.[40,54]

The increased pain levels for women were seen regardless of other symptoms, stress, presence of articular noises, bruxism, and reduced mouth opening. This is consistent with the results of several studies using various methodologies. Women show more pronounced pain responses to experimentally induced stimuli than men[25–29,55–59] and also increased pain and reflex responses to glutamate application to jaw muscles.[60,61] In females, central processing of nociceptive signals may reflect a nociceptive neuronal hyperexcitability.[62] Evoked pain will also persist longer in females,[63] and repetitive mechanical pain stimuli show greater temporal summation of evoked noxious stimuli than in males. This effect can be demonstrated in healthy subjects and in patients with TMD.[62,64,65]

In their response to muscle palpation, female patients showed clearly a stronger reaction than male patients. This effect could also be observed regardless of subjective symptoms, stress, clicking and crepitation noises, bruxism, and extent of mouth opening. This may be due to the differences in muscles between men and women. Rankin et al described significant sex-specific differences in the size and shape of neck muscles.[66] Females with similar training status show a lesser degree of muscular protection for ligaments in the knee as compared to males.[67] Females and males also differ in their share of different muscle fiber types[21,23]; while females show larger shares of type I fibers, the opposite is true for type II fibers. Compared to men, women tire slower in muscular endurance testing[68] and show increased pain and jaw muscle reflex responses to glutamate application to jaw muscles.[60,61] In addition, women are more at risk than men for the development and chronification of musculoskeletal pain.[69] In this study, the increased muscular problems also resulted in the more frequent prescription of physiotherapeutic measures in female patients.

This study had several strengths, in particular the unselected consecutive patient sample reflecting the population seeking medical advice and treatment of TMD. Furthermore, all patients were assessed with a standardized protocol by a small number of experts. Limitations were the retrospective design and the fact that the protocol followed was not specifically designed to explore sex differences.

Sex aspects are of increasing importance in many medical disciplines. The goal of the present study of TMD patients was to evaluate sex differences in reported orofacial pain and pain on palpation and to explore the relationship between clinical as well as individual features and pain with the intention to detect a potential moderating effect of sex. There are many studies indicating that being female is a risk factor for the development of TMD,[47,70] but there have been no attempts to date to explain this increased risk based upon patients' attributes. Although various factors such as bruxism, self-reported stress, or the degree of suffering were analyzed, none had a modifying effect on the difference in pain intensity between males and females. Assuming that a certain level of pain associated with TMD is necessary to seek medical advice, a large part of the difference in the prevalence of males and females could be due to reported pain sensitivity. As a consequence, pain management should be included in the therapeutic program of TMD patients from the very beginning and especially in female patients. Since women have a higher risk for chronification of pain and also higher pain intensity among chronic pain patients, an interdisciplinary cooperation in treatment could be successful.[71] Women could benefit more than men from multimodal pain management.[72] Furthermore, more resources to adequately manage chronic pain conditions in women are required.[73] Future prospective trials including specific pain management could assess efficacy of such multifaceted therapeutic procedures.

In conclusion, the present study confirmed the assumption that, given similar clinical features, women subjectively experience more pain and more tenderness on palpation pressure than men. Stress represents a risk factor for the development of TMD in both males and females. In contrast to men, who had a more even age distribution, women show peaks of prevalence in the age group below 25 years and in the age group of 55 to 64 years.

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