Painful Temporomandibular Disorders Are Common in Patients with Postural Orthostatic Tachycardia Syndrome and Impact Significantly upon Quality of Life

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Aims: To explore the point prevalence of painful temporomandibular disorders (TMD) in a well-characterized clinical cohort of postural orthostatic tachycardia syndrome (PoTS) sufferers and to understand the functional and physiologic impact of this comorbidity on the patient. **Methods:** Patients with PoTS were retrospectively recruited from a previous study conducted in a UK hospital setting. Data had previously been collected on several parameters, including sociodemographic, physiologic, and functional. The participants were mailed a highly sensitive (99%) and specific (97%) self-report screening instrument for painful TMD. Simple descriptive statistics with Fisher Exact and Kruskal-Wallis tests were used to examine the data and draw inferences from it. **Results:** A total of 36 individuals responded (69% response rate). Just under half (47%) of the sample screened positive for painful TMD. There was no significant difference between the screening result for TMD or previously reported headaches or joint pain ($P > .05$). Chronic fatigue syndrome (CFS) was diagnosed by the Fukuda Criteria in 44% of the total sample and in 56% of those with painful TMD. There were no significant differences in physiologic parameters in CFS and TMD. TMD caused a significant decrease in quality of life as measured by the Patient-Reported Outcomes Measurement Information System, Health Assessment Questionnaire ($P < .05$). **Conclusion:** TMD are common in patients with PoTS. They have a significant, additional impact on patients' quality of life and should therefore be screened for at an early stage in PoTS. *J Oral Facial Pain Headache 2015;29:152–157. doi: 10.11607/ofph.1396*

Key words: *postural orthostatic tachycardia syndrome, quality of life, temporomandibular disorders*

Postural orthostatic tachycardia syndrome (PoTS) is a heterogeneous group of conditions characterized by orthostatic intolerance without associated hypotension. The orthostatic intolerance manifests itself within 10 minutes of standing as an increase in heart rate greater than 30 beats per minute or as a heart rate greater than 120 beats per minute.[1] Data from the United States suggest that PoTS affects 170 per 100,000 of the population and causes significant disability in most daily activities.[2] The same data suggest that up to a quarter of PoTS sufferers are so disabled by the condition they are unable to work.[3] More recent UK data suggest that females may be more frequently affected than males in the second to fourth decades of life and that levels of disability are similar to the US data.[4] PoTs has also been shown to often be comorbid with Ehlers-Danlos syndrome and chronic fatigue syndrome (CFS); excepting the use of beta-blockers, there is a lack of coherence in the approach to its treatment.[4]

Temporomandibular disorders (TMD) are a group of painful musculoskeletal conditions affecting the muscles of mastication, the temporomandibular joint, and/or its associated structures. TMD can present acutely, for instance, following a difficult tooth extraction or prolonged dental procedure, or can present with no easily identifiable cause; both types can progress to become chronic.[5]

Young females are the predominately presenting cohort of patients for treatment in both PoTS and TMD.[1,5] Both conditions have a significant impact on the patient's quality of life.[6–8] The underlying etiology of

both TMD and PoTS is uncertain but is likely to be of a biopsychosocial nature.[9,10] Common to both groups of conditions is an increasing body of evidence that implicates dysautonomia as part of the underlying pathophysiology.[11–14]

The central nervous system maintains homeostasis through the processing of inputs from many different sources including those related to autonomic, inflammatory, sensory, and psychological functions. TMD are known to contribute to a multisystem dysregulation, which amplifies pain within the nervous system.[15] Given this fact, the aim of the present study was to explore the point prevalence of painful TMD in a well-characterized clinical cohort of PoTS sufferers and to understand the functional and physiologic impact of this comorbidity on the patient.

Materials and Methods

Participants

In 2013, consecutive PoTS patients diagnosed according to recognized criteria[16] in the Falls and Syncope service at Newcastle-upon-Tyne Hospital NHS Foundation Trust were invited to provide details about the onset of their illness.[4] They were asked to identify whether they were willing to be invited to complete further symptom assessment tools to increase understanding of their condition. Of the 87 attending the outpatient clinic, 52 (60%) identified themselves as willing to participate in future assessments of symptom burden. All of the patients included had their diagnosis made by a secondary care clinician (details given below).

Study Design

This non-interventional study was conducted with the informed consent of all patients involved, and the local clinical governance committee of the National Health Service approved the methods of the original survey and also the method for gaining consent for research in the Falls and Syncope clinic.

A cross-sectional design was used to assess the presence of TMD at a single point in time in those responding. The TMD screening instrument[17] was mailed to those who identified themselves as willing to be included in future research in July 2013. A reminder was sent at 12 weeks. The Falls and Syncope service takes written informed consent for participation in research, audit, and service evaluation from all attending patients. Return of the completed instrument was taken as indicative of consent for use of the data.

Assessment of TMD

TMD were assessed using a validated, self-complete, six-item screening instrument with high sensitivity (99%) and specificity (97%) for painful TMD.[17] The first question is scored on a unipolar, ordinal, three-item response scale (No pain [0] Pain comes and goes [1] Pain is always present [2]) and the remaining five questions are scored on a dichotomous response (No [0] Yes [1]). All questions enquire about signs and symptoms of painful TMD. A summary score is generated by summing the response codes and the threshold value for a positive screen is greater or equal to three.

Symptom Assessment Tools

The process and instruments used have been fully explained and documented previously,[4] but briefly the patient's history and sociodemographics were recorded along with their responses to the following five validated symptom assessment tools.

Fatigue Impact Scale (FIS). Fatigue is a recognized complication of PoTS. The FIS is a 40-item tool that assesses patients' perception of the impact of fatigue on physical, psychosocial functions. Each item is scored 0 (no problem) to 4 (extreme problem). The total score is calculated by adding together the response to each of the 40 questions. Higher scores indicate greater impact of fatigue on function.

Hospital Anxiety and Depression Scale (HADS). The HADS is a 14-item scale optimized for use in patients with chronic disease. Seven of the items relate to anxiety and seven relate to depression. Each item has four response options, which score either 0, 1, 2, or 3, with higher scores indicating greater anxiety or depression. Items are summed within the relevant subscale (anxiety or depression) to give a total score. Higher scores indicate greater anxiety or depression.

Patient-Reported Outcomes Measurement Information System, Health Assessment Questionnaire (PROMIS-HAQ). The PROMIS-HAQ assesses the functional and physical ability of subjects. It consists of 20 items that ask patients to rate their ability to carry out daily activities on a five-point scale of "0 = without any difficulty" to "4 = unable to do." Higher scores indicate worse functional ability and therefore greater functional impairment.

Epworth Sleepiness Scale (ESS). The ESS assesses daytime somnolence. Participants are asked how likely they are to doze off in eight commonly encountered situations. Responses range from 0 (would never doze off) to 3 (highly likely to doze off). Higher scores indicate greater sleepiness. Scores greater than 9 indicate excessive daytime somnolence.

Composite Autonomic Symptoms Scale (COMPASS). Autonomic dysfunction was also assessed using the COMPASS, which consists of 73 questions assessing autonomic symptoms that are scored on the basis of presence, severity, distribution, frequency, and progression. Twenty-four individual scores are

Table 1 Cross-Tabulation of TMD Screening Results Against Symptoms of Headache and Joint Pain Predating Development of PoTS Symptoms

Symptoms	TMD screening result, % of sample (n)		
	Negative	Positive	Total
Headaches			
None reported	36 (13)	25 (9)	61 (22)
Reported	17 (6)	22 (8)	39 (14)
Total	53 (19)	47 (17)	100 (36)
Joint pain			
None reported	25 (9)	19 (7)	44 (16)
Reported	28 (10)	28 (10)	56 (20)
Total	53 (19)	47 (17)	100 (36)

P > .05 Fisher exact test for both cross-tabulations.

Table 2 Work Status in Relation to TMD Screening Result

Work status	TMD-negative screen (n)	TMD-positive screen (n)	Total (n)
On disability	1.0	7.0	8.0
Student	2.0	1.0	3.0
Homemaker*	2.0	1.0	3.0
Retired	3.0	2.0	5.0
Unemployed	4.0	3.0	7.0
Working part-time	5.0	0.0	5.0
Working full-time	2.0	3.0	5.0

P > .05 Fisher exact test.
*Housewife or Househusband—individual chooses to stay at home either to help with childcare or upkeep of the home.

Table 3 Frequency of CFS Diagnosis and Mean Age in Relation to TMD Screening Result

Screening result	Male (n)	Female (n)	Mean age, y (SD)
TMD negative/ CFS negative	2	10	38 (± 12)
TMD negative/ CFS positive	3	4	38 (± 12)
TMD positive/ CFS negative	1	7	35 (± 10)
TMD positive/ CFS positive	1	8	32 (± 7)

CFS = chronic fatigue syndrome.

then summed to provide an indicator of total overall symptom burden (total COMPASS score). Higher scores indicate more severe symptoms.

Physiologic Assessment

As part of routine clinical assessment, patients referred to the clinic undergo formal autonomic assessment. All patients are asked to refrain from smoking and caffeine ingestion on the day of clinic attendance and are advised to eat a light breakfast only. All investigations were performed in the morning and took place in a warm, quiet room.

After resting in the supine position for 10 minutes, subjects were asked to assume a standing position as quickly as possible without assistance and maintain this position for 3 minutes or as long as possible. Cardiovascular assessments were carried out with continuous heart rate and beat-to-beat blood pressure measurement (Task Force, CNSystems). Data were digitized and stored offline. Baseline measurements were taken as an average for 20 beats in supine position immediately prior to standing. Orthostatic heart rate change was the change in mean heart rate from baseline to heart rate on standing. The absolute maximum heart rate on standing was also recorded. PoTS was diagnosed using recognized diagnostic criteria[18] and was defined as an increase in heart rate from the supine to upright position of >30 beats per minute (beat to beat) or to a heart rate of >120 beats per minute on immediate standing or during the 3 minutes of standing.

Data Analysis

Both Excel (Excel v10, Microsoft Corporation) and Stata (StataCorp 2011, Stata Statistical Software: Release 12) were used for the analysis of data. Simple descriptive statistics were used to assess the differences between groups, and nonparametric inferential statistical tests were used ($\alpha = .05$) to examine the statistical significance of any differences.

Results

A total of 36 individuals responded from those involved in the previous study (52 cohort; 69% response rate). Those responding were predominately female (81%) Caucasians (100%) with a mean (± SD) age of 36 (± 10) years and did not significantly differ from the original cohort on the basis of gender, ethnicity, or age (*P* > .05, Mann-Whitney).

The mean age at which symptoms started was 28 (± 12) years and diagnosis of PoTS was made at age 33 (± 10). Some individuals reported (general) joint pain (56%) and/or headache (39%) that predated the start of PoTS symptoms. A total of 17 individuals (47%) screened positive for TMD. These individuals had a mean age of 33 (± 9) years, as opposed to those without a positive TMDs screen who had a mean age of 38 (± 12) years (*P* > .05, Mann-Whitney). In the cohort examined, two individuals (6% of whole cohort) suffered from Ehlers-Danlos syndrome; both of these individuals screened positive for TMD (12% of those screening positive).

Table 1 gives a cross-tabulation of the TMD screening results against pre-existing headache and generalized joint pain. Table 2 shows current work status of the cohort examined. When comparing the group screening negative for TMD with the group

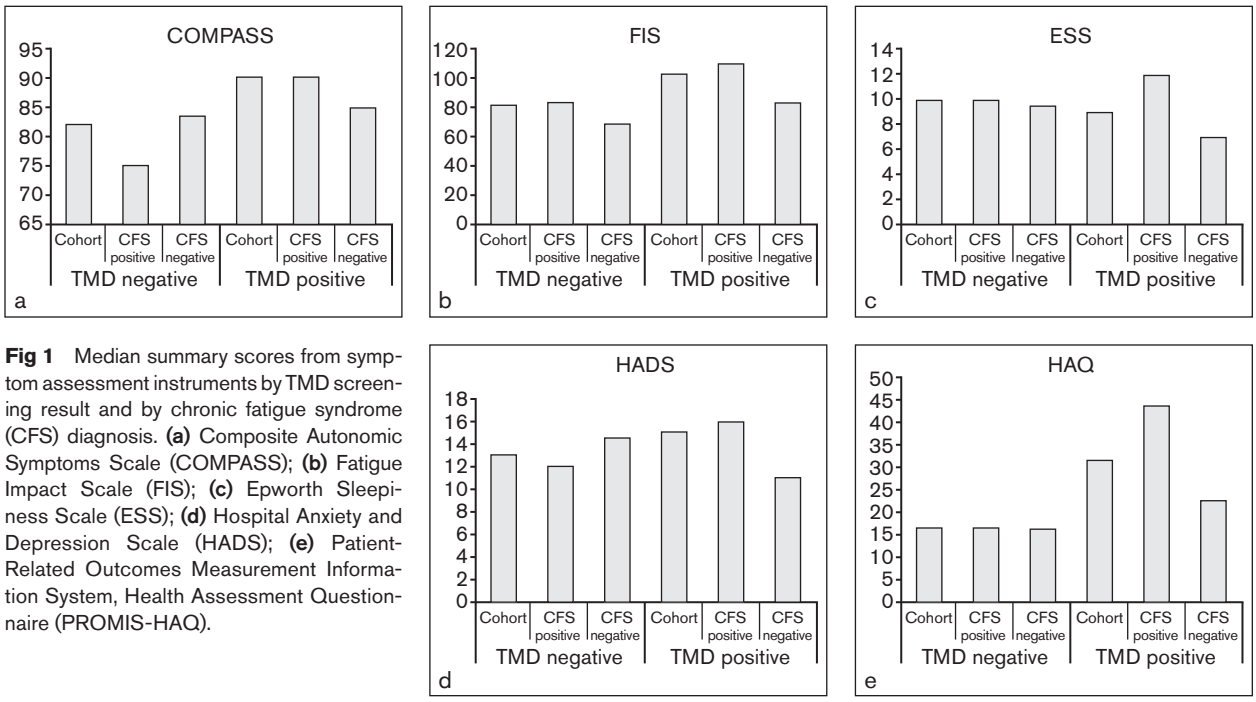

Fig 1 Median summary scores from symptom assessment instruments by TMD screening result and by chronic fatigue syndrome (CFS) diagnosis. **(a)** Composite Autonomic Symptoms Scale (COMPASS); **(b)** Fatigue Impact Scale (FIS); **(c)** Epworth Sleepiness Scale (ESS); **(d)** Hospital Anxiety and Depression Scale (HADS); **(e)** Patient-Related Outcomes Measurement Information System, Health Assessment Questionnaire (PROMIS-HAQ).

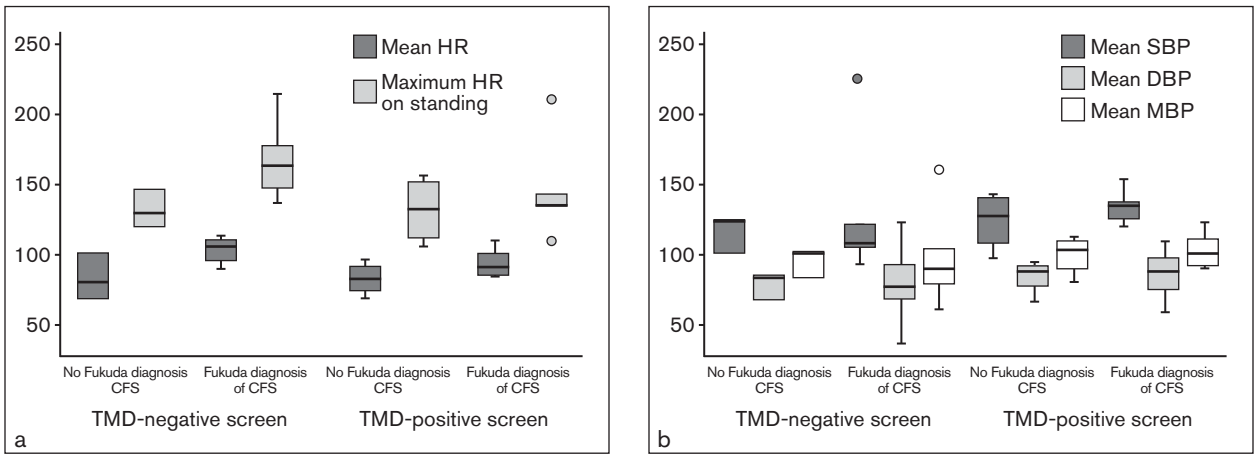

Fig 2 Box plots of physiologic parameters of the sample. **(a)** Mean heart rate (HR) and maximum heart rate on standing. **(b)** Mean blood pressure: systolic (SBP), diastolic (DBP), and mean (MBP).

screening positive for TMD, higher unemployment levels and less time spent on social (mean 3 ± 4 hours as compared to 6 ± 5 hours) and household activities (mean 4 ± 3 hours, as compared to 12 ± 17 hours) were identified in those screening positive for TMD. None of these differences, however, reached statistical significance ($P > .05$, Mann-Whitney).

Just under half of the PoTS sample (44%) had received a Fukuda diagnosis of CFS (Table 3). There was no significant difference ($P > .05$, Fisher exact test) between the prevalence of TMD in those with or without a diagnosis of CFS. Two individuals also reported systemic conditions that would cause myogenous pain ("myofascial pain syndrome," and fibromyalgia). CFS-positive individuals only accounted for two out of the seven individuals with a positive screening for TMD who were unemployed.

The median scores for the symptom assessment instruments used with the cohort are shown in Figs 1a to 1e. There was a significant difference between the scores of those screening positive for TMD (median 31.25 [interquartile range (IQR) 18.75–45]) and those screening negative for TMD (median 16.25 [IQR 6.25–22.5]) on the PROMIS-HAQ ($P = .01$ Mann-Whitney). This shows an increased difficulty in performing daily activities as shown by the PROMIS-HAQ between those screening positive for TMD and those who do not. The box-plots for the physiologic measurements conducted with the participants are shown in Figs 2a and 2b. There were no significant

differences between groups in their physiologic parameters ($P > .05$, Kruskal-Wallis).

Discussion

TMD were found to be prevalent in the sample investigated in the present study, with the point prevalence being 47%. The prevalence of TMD in this cohort adds further support to the conditions having a similar underlying dysautonomic pathophysiology. Despite the lack of a significant difference between the levels of dysautonomia between those screening positive and those screening negative for TMD, there appeared to be a trend toward higher levels of dysautonomia for positive subjects on the COMPASS scale. It may be that individuals with more than one dysautonomic condition suffer proportionally greater levels of autonomic nervous system dysfunction, although this cannot be proven within the constraints of the present sample. If this were proven to be the case, it could have implications for therapy especially in TMD, where a recent proof-of-concept trial has found subtherapeutic levels of propranolol effective in reducing pain.[19] On the basis of this recent evidence, clinicians might chose to adjust their pharmacologic management of chronic TMD and primarily focus on attempting to control the dysautonomia in patients who have multiple conditions known to affect the autonomic nervous system. This is opposed to pharmacologically managing chronic TMD with the usual array of neuromodulatory agents,[20–22] which have several undesirable side effects both for a PoTS population and for a CFS population.

Those individuals in the present sample with comorbid TMD seemed to experience a greater impact on their everyday lives. Although not statistically significant, there were more individuals on disability allowance (receiving government assistance due to inability to work) and more individuals spending less time in social and household activites with a positive screening for TMD. This impact is mirrored by the results of the PROMIS-HAQ questionnaire, where there was a significant difference between those with a positive TMD screening result compared to those with a negative screening result, the former demonstrating a markedly increased level of functional impairment in daily activities. This is consistent with findings that suggest TMD exert a profound biopsychosocial impact on quality of life[23,24] even when present as the only morbidity. Trends seen on the HADS also seem to demonstrate a slightly higher depression and anxiety status for those screening positive for TMD when compared to the TMD-negative cohort, which is also consistent with known association of TMD with anxiety and depression.[25,26] Within the constraints of this study and its design, it is difficult to examine in depth the additional effect of TMD on quality of life in order to explain whether it is an additive or multiplicative effect. This said, however, there appears to be a significant effect on quality of life, and given that those with a positive screen for TMD tended to be of a younger age, this decrease in quality of life may potentially extend over a longer period.

The lack of association between objective measures of autonomic function, including heart rate on standing, seems to suggest that objective assessment does not have utility as a clinically applicable tool to differentiate between PoTS patients with and without TMD. The same lack of association seems to suggest from these data that increased autonomic symptom burden in PoTS patients with TMD (increased COMPASS scores) is not associated with changes in objective measures. COMPASS is a broad-based autonomic symptom measure that considers autonomic symptoms across a range of domains, whilst the objective parameters considered in this study focused on cardiovascular responses to standing. It is possible, therefore, that some of the differences seen in those with and without TMD are related to differences in autonomic symptoms outside the cardiovascular system.

The limitations of this study were its retrospective nature and small sample size. Essentially this study utilized a self-selecting, convenience sample that did not undergo expert examination for TMD and its subtype, or focus on whether individuals had experienced previous treatment for TMD. There were also two cases of Ehlers-Danlos syndrome in the cohort examined, but it is possible that either subclinical or undiagnosed cases existed within the cohort. Ehlers-Danlos syndrome is known to be associated with arthrogenous TMD[27] and therefore could influence the prevalence of TMD on screening. The results of this study should, therefore, be interpreted with caution, but at the same time the results do point to the need to undertake a larger prospective study examining the impact of TMD in PoTS. This study would need to examine possible confounding factors such as *(1)* the impact of age at diagnosis, which in turn may affect whether the diagnosis has impacted upon employment or disability; *(2)* the presence or absence of TMD at the point in time of the questionnaire, as TMD can fluctuate in severity and may, therefore, lead to false positives or negatives; and *(3)* the presence of Ehlers-Danlos syndrome.

The authors believe a further broader-prospective study is merited given the fact that TMD patients can respond favorably if treated with simple conservative measures early enough in their presentation.[5,28] Therefore, it may be possible to reduce the burden of suffering for those with PoTS through simple, noninvasive means if TMD are identified early. If TMD are left undiagnosed or untreated, however, central sensitization[29,30] may occur and could worsen the pain and prognosis for the patient.

Conclusions

TMD are a prevalent comorbidity in PoTS patients and exert a negative impact on patients' quality of life. Screening for TMD in PoTS patients by using the simple screening instrument cited in this study would be useful for identifying those who suffer from TMD early so that they may receive early, simple, noninvasive management of their TMD. The outcome of such treatment should be carefully monitored to determine if PoTs patients respond similarly to other TMD patients.

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