Composite Autonomic Symptom Score 31 (COMPASS-31) for the assessment of symptoms of autonomic dysfunction in fibromyalgia

F. Salaffi, S. Farah, M.G. Lommano, B. Bianchi, M.C. Mangiafico, M. Di Carlo

Rheumatology Unit, Dipartimento di Scienze Cliniche e Molecolari, Università Politecnica delle Marche, Carlo Urbani Hospital, Jesi, Italy.

Abstract

Objective

Autonomic dysfunction is a feature of fibromyalgia (FM). The Composite Autonomic Symptom Score-31 (COMPASS-31) is a validated tool to assess autonomic dysfunction. This study aimed to evaluate autonomic dysfunction in FM patients using COMPASS-31 and examine correlations with FM severity measures.

Methods

A cross-sectional study included women with FM and matched healthy controls. Participants completed COMPASS-31, the Revised Fibromyalgia Impact Questionnaire (FIQR), Polysymptomatic Distress Scale (PDS), Modified Fibromyalgia Assessment Status (FASmod), and PainDetect Questionnaire (PDQ). Correlations and severity analyses were performed.

Results

The study included 77 women with FM and 77 matched controls. Autonomic dysfunction was observed in 64.9% of FM patients and 3.5% of healthy controls. FM patients exhibited significantly higher COMPASS-31 scores (mean 47.03±17.27) compared to controls (21.55±11.48; p<0.00001). Internal consistency was good (Cronbach's α=0.74). A COMPASS-31 cut-off point of 38.28 (sensitivity 71.43%; specificity 91.86%; LR+ 8.78) distinguished FM patients from healthy controls. COMPASS-31 scores correlated positively with FIQR (rho=0.47, p<0.0001), PDS (rho=0.36, p<0.0001), FASmod (rho=0.32, p=0.004) and PDQ scores (rho=0.56, p<0.0001). Disease severity categories identified by FIQR were significantly associated with autonomic dysfunction symptoms (Kruskal-Wallis test: 18.77; p=0.00086).

Conclusion

This study highlights the high prevalence of autonomic dysfunction in FM and supports the utility of COMPASS-31 as a reliable tool for assessing autonomic symptoms in FM patients. Future research should explore the causality and the impact of FM severity on autonomic dysfunction through longitudinal studies.

Key words

fibromyalgia, COMPASS-31, autonomic dysfunction, autonomic nervous system

Fausto Salaffi, MD, PhD
Sonia Farah, Eng
Maria Giovanna Lommano, MD
Benedetta Bianchi, MD
Maria Chiara Mangiafico, MD
Marco Di Carlo, MD

Please address correspondence to:
Marco Di Carlo
Clinica Reumatologica,
Università Politecnica delle Marche,
Ospedale Carlo Urbani,
Via Aldo Moro 25,
60035 Jesi (AN), Italy.
E-mail: dica.marco@yahoo.it

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ORCID iDs
F. Salaffi: 0000-0002-3794-6831
S. Farah: 0000-0002-9815-2621
M.G. Lommano: 0009-0000-6719-8021
B. Bianchi: 0000-0002-0362-0825
M.C. Mangiafico: 0009-0003-0597-0698
M. Di Carlo: 0000-0002-0906-4647

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Introduction

Fibromyalgia (FM) is a chronic pain syndrome affecting 2.2% of the general population (1). In addition to musculoskeletal pain, FM is characterised by neurological symptoms, fatigue, sleep disturbances, abdominal discomfort, and exercise intolerance (2). Due to its symptoms, distress, and disability, without clear structural damage, FM is classified as a functional syndrome (3).

The pathophysiology of FM has been extensively studied, highlighting a multifactorial origin. Several mechanisms have been proposed, including genetic predisposition, alterations in neurotransmitters (4), hormonal imbalances in the hypothalamic-pituitary-adrenal axis, oxidative stress, impaired pain modulation, central sensitisation, and autonomic nervous system (ANS) dysfunction (5). Despite uncertainties regarding whether dysautonomia is a cause, consequence, or component of this condition, it may represent a key factor in FM pathogenesis (5-7).

The ANS influences physiological responses essential for stress management, and its dysfunction may exacerbate pain and other FM symptoms (8). The Composite Autonomic Symptom Score-31 (COMPASS-31) is a validated and simplified tool developed from the original Autonomic Symptom Profile (ASP) (9, 10). It evaluates six weighted domains of autonomic function, respectively orthostatic intolerance, vasomotor, secretomotor, gastrointestinal, bladder, and pupillomotor, yielding a total score where higher values indicate more severe dysfunction (10).

Previous research using COMPASS-31 in FM patients has confirmed a high prevalence of autonomic dysfunction symptoms unrelated to pain, supporting its utility in evaluating autonomic symptoms in FM (6, 11). These findings align with the hypothesis that dysautonomia may amplify symptom severity through mechanisms such as altered vascular tone, impaired gastrointestinal motility, and abnormal blood pressure regulation (5, 7).

Given the complexity of FM, assessing dysautonomia alongside other validated measures may provide deeper insights into symptom burden and disease severity. Tools such as the Revised Fibromyalgia Impact Questionnaire (FIQR), the Polysymptomatic Distress Scale (PDS), the Modified Fibromyalgia Assessment Status (FASmod), and the PainDetect Questionnaire (PDQ) (12-15), are traditional instruments aimed to assess disease severity and neuropathic pain features in FM. The metric validity of the COMPASS-31 in relation to the aforementioned indices of disease severity remains an underexplored topic to date.

Starting from these considerations, this study aimed to evaluate the prevalence of autonomic dysfunction in FM patients, compared to age- and sex-matched controls, using COMPASS-31. Additionally, it sought to determine whether COMPASS-31 scores correlate with established FM severity measures, including FIQR, PDS, FASmod, and PDQ.

Methods

Study design and participants

This was a cross-sectional study conducted at the outpatient clinic of the Rheumatology Unit of the Università Politecnica delle Marche, "Carlo Urbani" Hospital, Jesi (Ancona), Italy. Participants were recruited during routine clinical visits. The study included women with FM who met the 2016 revised American College of Rheumatology (ACR) criteria for FM (16). The clinical practice followed the European Alliance of Associations for Rheumatology (EULAR) guidelines for FM management (17). Written informed consent was obtained from all participants. Approval was granted by the Marche Regional Ethics Committee (CERM) (no. 1970/AV2).

Inclusion and exclusion criteria

FM diagnosis was confirmed by a rheumatologist with over ten years of experience. Exclusion criteria included major depressive disorder, severe anxiety, uncontrolled diabetes (HbA1c≥9%), uncontrolled hypertension, untreated hypo- or hyperthyroidism, respiratory or neurological illness, chronic kidney or liver disease, substance abuse within the past two years, cancer within the last five years, ongoing chemotherapy, eating disorders within the last five years, and other rheumatological diseases causing

secondary FM. Patients with incomplete data collection were also excluded.
For comparison, age, sex, and body mass index (BMI) matched healthy controls were enrolled. Healthy controls were recruited from hospital staff and patients' companions.

Assessments and questionnaires
Participants completed questionnaires addressing sociodemographic data, disease duration, and quality of life. The following instruments (the format of the instruments is available as Supplementary Material) were used to assess FM-related symptoms.

- COMPASS-31
The COMPASS-31 is a 31-item, self-administered questionnaire designed to evaluate symptoms of autonomic dysfunction across six weighted domains (10, 19): 1) orthostatic intolerance (10 points) evaluates dizziness, lightheadedness, and fainting episodes upon standing; 2) vasomotor dysfunction (6 points): assesses temperature regulation and abnormal sweating; 3) secretomotor dysfunction (7 points): measures issues related to dry eyes, dry mouth, and sweat secretion; 4) gastrointestinal dysfunction (28 points): captures symptoms like bloating, nausea, constipation, diarrhea, and satiety; bladder dysfunction (9 points): evaluates urinary urgency, frequency, and incontinence; 6) pupillomotor dysfunction (15 points): examines visual disturbances, including difficulty adjusting to light and focusing.
Responses are weighted based on symptom frequency, severity, and impact. The total score ranges from 0 to 100, with higher scores indicating more severe autonomic dysfunction. This tool has demonstrated reliability and validity for use in FM populations (6, 11).

- FIQR
The FIQR is an improved version of the original Fibromyalgia Impact Questionnaire, specifically designed to assess the overall impact of FM on patients' lives (12, 20). It is structured into three main domains: function, overall impact, and symptoms. The function domain evaluates the ability to perform daily activities, such as walking, cooking, and shopping. The overall impact domain measures how FM affects work productivity, personal relationships, and emotional well-being. The symptoms domain captures the severity of pain, fatigue, stiffness, sleep disturbances, anxiety, and depression. The final score ranges from 0 to 100, with higher scores reflecting greater disease impact. Severity levels are classified as remission (0–23), mild (24–40), moderate (41–63), severe (64–82), and very severe (83-100), providing a standardised framework for interpretation (21, 22).

- FASmod
The FASmod offers a multidimensional evaluation of FM severity (14, 23). It combines two sections: the first addresses fatigue and unrefreshing sleep over the previous week, rated on 0–10 numerical scales, with a maximum score of 20. The second section maps pain distribution across 19 anatomical areas, where each affected region scores one point, yielding a maximum score of 19. The total score ranges from 0 to 39, with predefined cut-off points categorising severity into remission (0-12), mild (13-20), moderate (21-18), severe (29-33), and very severe (34-39) disease states (21, 22). This tool provides a practical and quantitative measure for both clinical and research purposes.

- PDS
The PDS quantifies symptom severity of FM based on two components: the Widespread Pain Index (WPI) and the Symptom Severity Scale (SSS) (18). The WPI evaluates the number of painful body regions, with a maximum score of 19, while the SSS rates fatigue, cognitive impairment, and sleep disturbances on a scale of 0–12. Combined, these measures produce a total score ranging from 0 to 31. Severity is classified into remission (0–5), mild (6–15), moderate (16–20), severe (21–25), and very severe (26–31), enabling a detailed assessment of symptom burden and allowing the diagnosis of FM according to ACR (21, 22).

- PDQ
The PDQ is a validated tool for identifying neuropathic pain features in FM patients (15, 24). It consists of nine items evaluating sensory abnormalities, pain characteristics, and temporal patterns. Score ranges from -1 to 38, with thresholds distinguishing the likelihood of neuropathic pain: scores below 12 suggest it is unlikely, scores between 13 and 18 indicate a possible neuropathic component, and scores above 19 suggest a high probability. This tool complements other measures by isolating neuropathic symptoms, which may require targeted therapeutic approaches.

Statistical analysis
Descriptive statistics were used to summarise demographic and clinical data. Continuous variables were expressed as mean and standard deviation (SD) or as median and interquartile range (IQR) when data were not normally distributed. Categorical variables were presented as frequencies and percentages. Differences between FM patients and healthy controls were evaluated based on the distribution of the data. For normally distributed continuous variables, comparisons were conducted using Student's t-test. When the normality assumption was violated, the non-parametric Mann-Whitney U-test was applied. Categorical variables were analysed using the chi-square (χ^2) test or Fisher's exact test, as appropriate, to account for small sample sizes. The internal consistency of the COMPASS-31 questionnaire was assessed using Cronbach's α coefficient (25). A value of Cronbach's $\alpha \geq 0.70$ was considered acceptable, indicating a good level of reliability within the domains of the scale. To determine the optimal COMPASS-31 score threshold for identifying FM patients from healthy controls, ROC curve analysis was performed. The Youden Index was calculated to define the cut-off point that maximised sensitivity and specificity. Diagnostic accuracy was assessed using the area under the curve (AUC), where values >0.7 indicated adequate discrimination and values >0.8 reflected excellent discrimination (26, 27). Sensitivity, specificity, positive likelihood ratio (LR+), and negative likelihood ratio (LR–) were reported along

Table I. Descriptive characteristics of clinimetric analysis of the FM patients.

	Mean	Median	SD	IQR
FIQR total	63.06	63.00	18.02	58.86 - 65.33
FIQR overall status domain	12.05	12.00	5.00	9.00 - 16.00
FIQR physical domain	17.40	18.00	6.48	12.75 - 22.00
FIQR symptom domain	32.83	33.00	8.39	28.75 - 39.25
PDS	18.22	18.00	4.82	15.00 - 22.00
FASmod	24.70	25.00	6.11	21.50 - 30.00
PDQ	19.63	20.00	7.05	14.00 - 25.25
COMPASS-31 total	47.03	46.59	17.27	30.79 - 62.05

SD: standard deviation; IQR: interquartile range; FIQR: Revised Fibromyalgia Impact Questionnaire; PDS: Polysymptomatic Distress Scale; FASmod: Modified Fibromyalgia Assessment Status; PDQ: PainDetect Questionnaire; COMPASS-31: Composite Autonomic Symptom Score-31.

with their 95% confidence intervals (CI). Spearman's rank correlation coefficients (rho) were used to examine associations between COMPASS-31 scores and other clinimetric measures, including the FIQR, FASmod, PDS, and PDQ. Correlation strength was interpreted as follows: 0.00–0.19: very weak; 0.20–0.39: weak; 0.40–0.59: moderate; 0.60–0.79: strong; 0.80–1.00: very strong. To assess whether autonomic dysfunction correlated with FM severity, participants were stratified into severity categories based on their FIQR scores. The Kruskal-Wallis test, a non-parametric method, was used to detect differences across severity levels. *Post-hoc* pairwise comparisons were conducted using Dunn's test, with Bonferroni corrections applied to control for multiple testing. All tests were two-tailed, and *p*-values less than 0.05 were considered statistically significant.

All statistical analyses were performed using MedCalc® software (v. 20.07; MedCalc Software, Mariakerke, Belgium).

Results

The study included 77 female patients with FM, with a mean age of 52.36 (±9.34) years and a mean disease duration of 6.2 (±4.0) years. A group of 77 healthy women (mean age: 58.1 years) served as control. Among the FM patients, 75.3% were married, and most had completed at least a high school education. On average, FM patients were moderately overweight, with a mean BMI of 26.20 (±2.69) kg/m^2. No significant differences were detected between FM patients and controls in terms of BMI.

Disease severity, as measured by FIQR, revealed a mean score of 63.06 (±18.02). Parallel assessments indicated a mean score of 18.22 (±4.82) for the PDS, 24.70 (±6.11) for the FASmod, and 19.63 (±7.05) for the for the PDQ (Table I).

FM patients exhibited significantly higher COMPASS-31 total scores compared to controls, with a mean score of 47.03 (±17.27) *versus* 21.55 (±11.48) ($p<0.00001$) (Table II). These differences were reflected across all specific domains of the COMPASS-31, where FM patients consistently reported higher symptom burdens. Orthostatic intolerance emerged as one of the most pronounced areas of dysfunction, with scores that were substantially elevated compared to controls ($p<0.00001$). Similar trends were observed for bladder dysfunction ($p<0.0001$), gastrointestinal disturbances ($p<0.0001$), pupillomotor symptoms ($p<0.001$), secretomotor dysfunction ($p<0.0001$), and vasomotor abnormalities ($p<0.00001$).

The internal consistency of the COMPASS-31, as evaluated by Cronbach's α coefficient, was 0.74, indicating good reliability in capturing autonomic symptoms across its domains.

A COMPASS-31 score threshold of 38.28, identified through ROC curve analysis, emerged as the optimal cut-off point in distinguishing patients with FM from healthy controls (Fig. 1). The AUC-ROC is 0.883 (95% CI 0.824 to 0.928, $p<0.0001$), the Youden index 0.633. At this threshold, 64.9% of FM patients (50 out of 77) and only 3.5% of controls (3 out of 86) were classified as having autonomic dysfunction. Diagnostic accuracy was supported by a sensitivity of 71.43%, specificity of 91.86%, and a positive likelihood ratio (LR+) of 8.78 (Table III).

The COMPASS-31 scores were further analysed in relation to disease severity measures, revealing significant correlations with the FIQR (rho=0.47, $p<0.0001$) (Fig. 2A), the PDS (rho=0.36, $p<0.0001$), and the FASmod (rho=0.32, $p=0.004$). The strongest relationship emerged between COMPASS-31 and PDQ scores (rho=0.56,

Table II. COMPASS-31 subdomain scores in healthy controls and FM patients.

	Groups								
	Healthy controls (n 77)				Fibromyalgia (n 77)				
	Mean	Median	SD	IQR	Mean	Median	SD	IQR	*p*
Orthostatic intolerance	4.26	0.00	6.93	0.00 - 12.00	15.27	16.00	12.92	2.50 - 25.00	<0.00001
Bladder dysfunction	1.07	1.11	1.26	0.00 - 2.22	2.06	1.111.89		1.11 - 3.33	<0.0001
Gastrointestinal disturbances	7.83	8.48	3.21	5.35 - 9.82	10.79	11.60	3.73	8.03 - 13.39	<0.0001
Pupillomotor symptoms	1.82	1.66	0.96	1.33 - 2.33	2.90	3.00	1.16	2.33 - 3.66	<0.001
Secretomotor dysfunction	4.15	4.28	3.49	0.00 - 6.42	7.96	8.57	3.33	6.42 - 10.71	<0.0001
Vasomotor abnormalities	1.82	0.00	4.02	0.00 - 0.83	7.77	2.50	11.93	0.62 - 4.16	<0.00001
COMPASS-31 total	21.55	21.66	11.48	11.59 - 28.98	47.03	46.59	17.27	30.79 - 62.05	<0.00001

SD: standard deviation; IQR: interquartile range; COMPASS-31: Composite Autonomic Symptom Score-31.

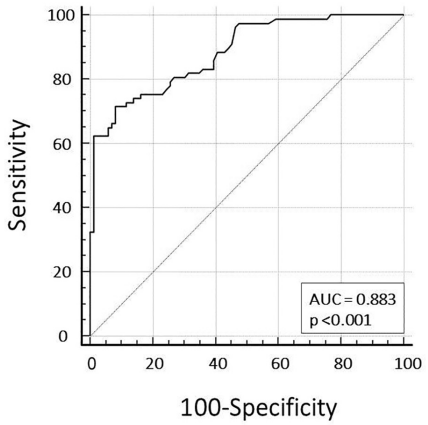

Fig. 1. Receiver operating characteristic (ROC) curve analysis showing the best threshold of COMPASS-31 in distinguishing FM patients from healthy controls (cut-off value of 38.28, sensitivity 71.4%, specificity 91.9, positive likelihood ratio 8.8).

p<0.0001) (Fig. 2B), suggesting a particularly close link between autonomic dysfunction and neuropathic pain features.

To better understand the role of autonomic dysfunction in relation to disease severity, patients were stratified according to FIQR scores. The Kruskal-Wallis test confirmed a statistically significant association between FIQR disease severity categories and COMPASS-31 scores (H=18.77; p=0.00086) (Fig. 3). Based on FIQR cut-off points for disease severity states (8 patients (10.4%) were classified as having very severe FM, 28 patients (36.4%) as severe, 34 patients (44.2%) as moderate, 4 patients (5.2%) as mild, and 3 patients (3.9%) as being in remission), the distribution of COMPASS-31 highlighted the variability of autonomic disfunction across the sample.

Discussion

This study demonstrated the high prevalence of autonomic dysfunction in patients with FM and provided broader clinimetric validation of the COMPASS-31 questionnaire for these patients. The correlation between COMPASS-31 and traditional disease severity indices confirms its validity as a tool, and its interpretative cut-off for distinguishing FM patients from healthy controls may be particularly useful in routine clinical practice.

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Table III. Criterion values and coordinates of the receiver operating characteristic curve analysis in identifying the COMPASS-31 cut-off value for the distinction between FM patients and healthy controls.

Criterion	Sensitivity	95% CI	Specificity	95% CI	LR+	LR-
>11.52	98.70	93.0 - 100.0	24.42	15.8 - 34.9	1.31	0.05
>18.54	98.70	93.0 - 100.0	40.70	30.2 - 51.8	1.66	0.03
>21.92	97.40	90.9 - 99.7	52.33	41.3 - 63.2	2.04	0.05
>22.27	90.91	82.2 - 96.3	54.65	43.5 - 65.4	2.00	0.17
>23.39	88.31	79.0 - 94.5	56.98	45.8 - 67.6	2.05	0.21
>24.19	88.31	79.0 - 94.5	59.30	48.2 - 69.8	2.17	0.20
>25.50	85.71	75.9 - 92.6	60.47	49.3 - 70.8	2.17	0.24
>27.25	83.12	72.9 - 90.7	63.95	52.9 - 74.0	2.31	0.26
>28.15	81.82	71.4 - 89.7	68.60	57.7 - 78.2	2.61	0.27
>29.27	75.32	64.2 - 84.4	76.74	66.4 - 85.2	3.24	0.32
>31.12	75.32	64.2 - 84.4	83.72	74.2 - 90.8	4.63	0.29
>32.66	74.03	62.8 - 83.4	86.05	76.9 - 92.6	5.31	0.30
>33.19	72.73	61.4 - 82.3	86.05	76.9 - 92.6	5.21	0.32
>35.83	72.73	61.4 - 82.3	88.37	79.7 - 94.3	6.25	0.31
>36.42	71.43	60.0 - 81.2	88.37	79.7 - 94.3	6.14	0.32
>38.28*	71.43	60.0 - 81.2	91.86	83.9 - 96.7	8.78	0.31
>39.77	64.94	53.2 - 75.5	94.19	87.0 - 98.1	11.17	0.37
>40.19	62.34	50.6 - 73.1	98.84	93.7 - 100.0	53.61	0.38
>57.34	32.47	22.2 - 44.1	98.84	93.7 - 100.0	27.92	0.68

CI: confidence interval; LR+: positive likelihood ratio; LR-: negative likelihood ratio.
*optimal cut-off point.

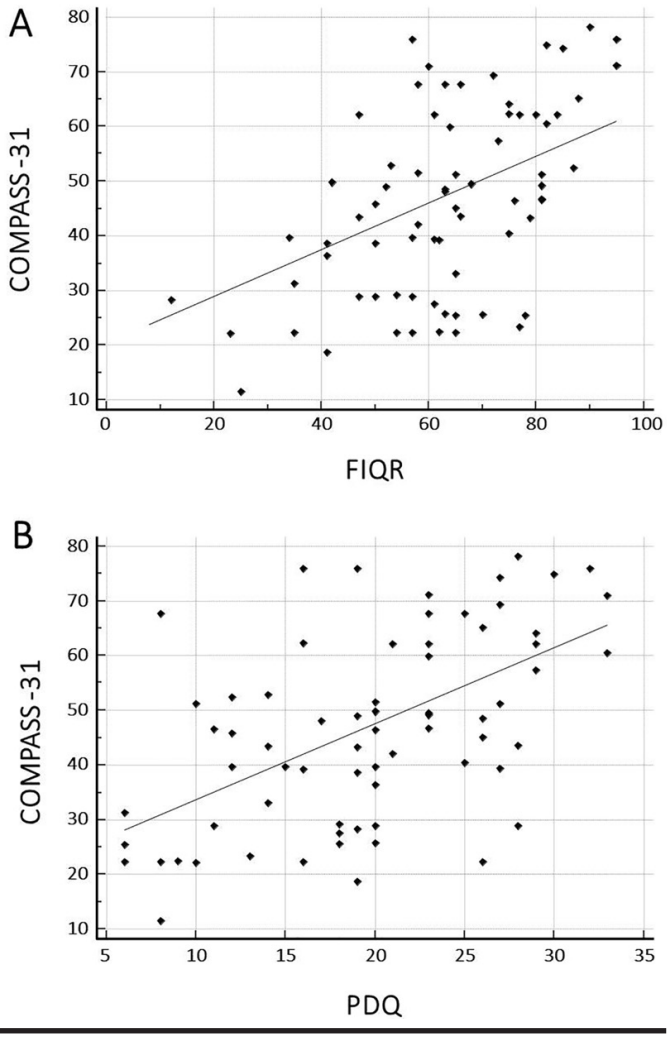

Fig. 2. Scatterplots showing the correlations (Spearman's rank correlation coefficient) between COMPASS-31 and FIQR (**A**), and between COMPASS-31 and PDQ (**B**) in FM patients.

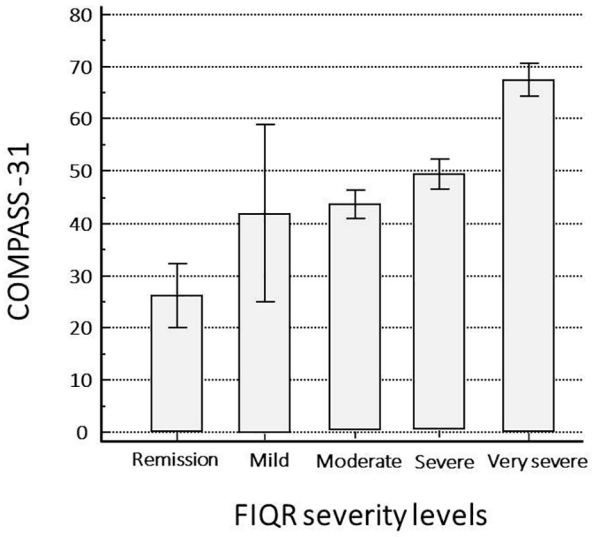

Fig. 3. Relationship between FIQR disease severity categories and autonomic symptom burden measured with COMPASS-31 (Kruskal-Wallis test 18.77; p=0.00086).

compass a wide range of tools capable of assessing disease severity (*e.g.* PDS, FIQR, FASmod) and pain (*e.g.* PDQ), in the specific domain of dysautonomia, the COMPASS-31 stands out as a nearly unique patient-reported outcome measure for evaluating this aspect. Since the diagnosis of FM remains a clinical exercise requiring the interpretation of symptoms, establishing an interpretative cut-off for this tool, applicable to FM, could aid clinicians in diagnosis, particularly in cases where there is uncertainty in assessing dysautonomic symptoms.

Despite extensive research, the aetiopathogenesis of FM remains uncertain, with evidence suggesting a multifactorial origin. Among proposed mechanisms, dysregulation of the ANS, particularly hyperactivity of the sympathetic nervous system (SNS), has been highlighted as a significant factor (28, 29).

Current evidence identifies three principal mechanisms contributing to FM pathophysiology: central sensitisation, temporal summation, and small fibre neuropathy. Temporal summation, involving endogenous excitatory pain pathways, occurs when repeated or continuous exposure to noxious stimuli amplifies pain perception, even without an increase in stimulus intensity (30, 31). Central sensitisation refers to an abnormal state of heightened responsiveness in spinal and supraspinal neurons, leading to hypersensitivity to low-threshold stimuli. This phenomenon often involves dorsal horn neurons, critical components in pain processing. Prolonged tonic stimulation of C-fibres can result in both short- and long-term hyperexcitability, thereby sensitising the nociceptive system and enhancing the perception of secondary pain stimuli, a process known as "wind-up" (32, 33).

Small fibre neuropathy is implicated in approximately 50% of FM cases (34-36). Patients with small fibre neuropathy commonly report intense burning pain, paresthesia, and allodynia due to the degeneration of small C-type nerve fibres (37). This degeneration may also underlie autonomic symptoms frequently observed in FM, including dry eyes and mouth, gastrointestinal disturbances, bladder dysfunction, and mechanical hypersensitivity, all of which substantially reduce quality of life. Evidence suggests that central sensitisation exacerbates these sensory abnormalities, underscoring its pivotal role in FM's sensory disturbances (38).

Although it remains unclear whether autonomic dysfunction is a primary cause, secondary effect, or merely a component of FM, patients consistently report more severe symptoms, including physical limitations and autonomic disturbances, compared to healthy controls (39, 40). Studies in Western populations estimate that autonomic dysfunction affects approximately 45% of FM patients (40). This dysfunction has been associated with sleep disturbances, fatigue, orthostatic intolerance, and an increased prevalence of syncope episodes (41, 42). These symptoms often lead to reduced physical activity and sedentary behaviour, contributing to physical deconditioning. Research indicates that FM patients primarily engage in light physical activity, spend more time in sedentary states than healthy controls, and are prone to physical deconditioning (43). For example, actigraphy studies reveal that while overall activity levels may be similar between FM patients and controls, those with FM engage in fewer high-intensity activities (43). Another study reported that FM patients spend an average of 10 hours per day, or 71% of their waking hours, in sedentary behaviours (44). Furthermore, FM patients exhibit reduced aerobic capacity, evidenced by an inability to sustain exercise above the anaerobic threshold or achieve maximal oxygen consumption during performance tests (45).

The evaluation of ANS function in clinical practice remains challenging due to the broad spectrum of autonomic symptoms. Traditional assessments such as heart rate variability (HRV) have identified altered autonomic profiles in FM, characterised by diminished parasympathetic activity and heightened sympathetic activity (46). However, HRV measurements are influenced by various confounders, including cardiac comorbidities, physical activity levels, breathing patterns, and medication use, potentially limiting their reliability. In contrast, the COMPASS-31 questionnaire provides a validated and standardised tool for assessing autonomic dysfunction and is particularly useful in evaluating FM-related autonomic symptoms (47, 48). A recent study has also documented, through a factor analysis, that the six domains of the COMPASS-31 can be summarised into three factors (49).

This study has certain limitations. The relatively small sample size may have reduced the statistical power to detect additional differences between FM patients and controls. Additionally, the absence of adjustments for multiple comparisons increases the risk of type I errors. However, given the exploratory nature of this study and the lim-

ited sample size, the prioritisation of potential clinical insights over stringent statistical adjustments was deemed appropriate. The single-centre design and inclusion of only female participants further restrict the generalisability of findings to broader and more diverse populations. Moreover, most participants presented with moderate-to-mild disease (53.2%), potentially influencing the outcomes. The exclusion of male participants also precludes conclusions about gender-based differences in disease severity and autonomic dysfunction.

Finally, the patient assessment did not include certain variables, such as physical exercise, which can impact dysautonomia.

In conclusion, this study underscores the elevate prevalence of autonomic dysfunction in FM, though its causal relationship, whether as a primary driver, secondary consequence, or integral component, remains unresolved. Recent findings, such as those reported by Ribeiro *et al*. (50), suggest that women with FM experience significant autonomic dysregulation. Given the association between autonomic dysfunction and increased cardiovascular risk and mortality (51), further research is essential to elucidate its long-term implications in FM patients. Future investigations should aim to clarify the role of ANS impairment in FM pathogenesis and assess the efficacy of targeted therapeutic interventions through rigorously designed clinical trials. Advancing knowledge in this area is critical for developing more effective treatment strategies and improving the quality of life for individuals with FM.

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