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ORIGINAL RESEARCH

Effects of Music Intervention on Pain, Mood, Sleep, and Heart Rate Variability in Patients with Chronic Pain: A Randomized Controlled Trial

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Background: Chronic pain (CP) represents the most prevalent form of pain experienced by patients. Among various conservative treatment modalities, music listening has emerged as a safe and effective strategy for pain management. However, the specific effects of music therapy (MT) on individuals with CP remain insufficiently understood. Therefore, this study aims to evaluate the efficacy of MT in patients with CP.

Methods: A total of 79 participants were randomly assigned to either the experimental group (EG) or the control group (CG). The EG received MT (receptive music listening) combined with health education, while the CG received health education alone. The primary outcome measure was the Simplified McGill Pain Questionnaire (SF-MPQ). Secondary outcome measures included the Patient Health Questionnaire-9 (PHQ-9), Generalized Anxiety Disorder-7 (GAD-7), the Pittsburgh Sleep Quality Index (PSQI), and heart rate variability (HRV). Assessments for the EG were conducted at baseline, immediately after the intervention, and two weeks post-intervention. The CG was assessed at baseline and two weeks post-intervention.

Results: Following treatment, the EG demonstrated significantly greater improvements in PHQ-9 scores and the low-frequency/high-frequency (LF/HF) ratio of HRV compared to the CG. Although both groups exhibited improvement over time, there were no statistically significant inter-group differences in total SF-MPQ scores post-intervention; however, the Present Pain Intensity (PPI) sub-score was significantly lower in the EG Furthermore, no significant inter-group differences were observed regarding anxiety or sleep outcomes.

Conclusion: Music listening was found to may alleviate pain severity in patients with CP. Additionally, our findings indicate that MT can effectively reduce depressive symptoms, a common and disabling complication among individuals with CP. Furthermore, the observed modulation of the LF/HF ratio suggests that MT may regulate the balance of sympathetic and parasympathetic nervous system activity in these patients. These results suggest that MT can serve as an effective adjunctive intervention in the management of CP.

Trial Registration: Registered in the Chinese Clinical Trial Registry (www.chictr.org.cn) on 01/06/2025 with the following code: ChiCTR-INR-2500095297.

Keywords: music therapy, chronic pain, heart rate variability, autonomic nervous

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Introduction

Chronic pain(CP) is typically defined as pain that persists or recurs for more than three months, leading to significant emotional disturbances and functional impairment in affected individuals.[1] Approximately 20% of adults in Europe experience CP,[2] and it is estimated that there are over 300 million individuals living with CP in China.[3] In addition to its substantial physical and emotional impact, CP imposes a significant economic burden on society. Current estimates

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indicate that annual expenditures related to CP exceed 200 billion euros in Europe and 150 billion dollars in the United States.[4]

Patients with CP are frequently affected by progressive autonomic symptoms. Anxiety, depression, and sleep disorders are among the most common complications observed in individuals with CP.[5] Non-steroidal anti-inflammatory drugs (NSAIDs) and opioids have traditionally been the primary pharmacological treatments for CP.[2,6–8] However, excessive use of NSAIDs is associated with an increased risk of adverse effects, including hypertension, arrhythmias, gastrointestinal disorders, and other related conditions.[9] In addition, due to concerns regarding the adverse effects and potential for addiction associated with opioids, a variety of novel non-pharmacological therapies are increasingly being explored as alternative treatment options.[10] Among these approaches, music intervention is regarded as one of the safest and most widely utilized non-pharmacological therapies for pain management, with a high level of patient acceptance.[11,12] Music therapy (MT) has been reported to affect the auditory centers of the brain, resulting in the effective suppression of adjacent pain centers and, consequently, significant alleviation of pain symptoms.[13] Furthermore, listening to music promotes the secretion of endorphins by the pituitary gland in the right hemisphere of the brain, thereby exerting analgesic effects. Concurrently, activation of midbrain nuclei, which are abundant in opioid substances, occurs. The impact of these opioids extends beyond mere pain alleviation, as they also substantially influence pain transmission between the prefrontal cortex and the limbic system.[14] Specifically, the melody and rhythm of music can influence the regulation of the autonomic nervous system (ANS) and pain perception by modulating activity in the limbic system and hypothalamus, ultimately leading to a reduction in catecholamine secretion.[15] In addition, musical stimuli are primarily processed by the amygdala and hippocampus, which are situated adjacent to the hypothalamic-pituitary axis at the core of the limbic system.[16] MT has also been shown to exert beneficial effects on anxiety, depression, pain, fatigue, physiological responses, and overall quality of life.[17,18] For example, music with frequencies in the 8–13 Hz range can stimulate alpha brain wave activity, thereby promoting psychological relaxation. Additionally, low-frequency music (16–150 Hz) has been shown to help alleviate pain and reduce stress.[19] MT is broadly categorized into two main modalities: active and receptive.[20] Active MT is defined as a multifaceted intervention that involves the patient's active participation in musical activities, such as singing, instrument playing, or composition. This therapeutic process integrates the patient's previous musical background while emphasizing new musical experiences acquired during assessment and treatment. In contrast, receptive MT is typically administered as an individual intervention. It does not require patients to actively engage in music-making; instead, the core approach focuses on listening to specific musical selections to evoke emotional expression. This modality serves as a continuous intervention aimed at helping patients overcome communication barriers, heighten awareness of emotional distress, and facilitate positive psychological transformation. Consequently, music therapists must ensure that the selected music is appropriate and conducive to the patient's well-being.[20] Research indicates that receptive MT can effectively enhance mood and modulate various psychophysiological components of pain.[21]

Abnormal autonomic nervous function is frequently observed during the progression of CP. Simultaneously, assessing the efficacy of interventions for CP by monitoring changes in objective physiological indicators has become an increasingly prominent focus in pain research.[22–24] Studies have demonstrated that both the sympathetic and parasympathetic nervous systems play integral roles in the regulation of pain.[25] Heart rate variability (HRV) analysis has been widely adopted as a standard method for assessing ANS function. In particular, the low-frequency (LF; 0.04–0.15 Hz) and high-frequency (HF; 0.15–0.4 Hz) spectral components of HRV serve as independent indicators for evaluating sympathetic and vagal (parasympathetic) activity, respectively.[26,27] In addition, studies have demonstrated that HRV is associated with depressive symptoms and insomnia.[28,29]

Despite the increasing focus on music intervention for the management of CP, existing research remains limited, particularly due to the scarcity of randomized controlled trials investigating the physiological effects of MT via HRV. Moreover, the majority of prior studies have relied heavily on subjective self-reports. To address these gaps, this study innovatively integrates subjective measures with objective HRV analysis to evaluate the efficacy of music intervention on pain severity, sleep quality, mood, and autonomic function in patients with CP.

Methods

Study Design

A single-blind, parallel-group trial with a two-week follow-up was conducted from January 2025 to June 2025. Blinding was maintained during the outcome assessment and data analysis phases. The study adhered to the principles of the Declaration of Helsinki and was approved by the Ethics Committee of Huadong Hospital Affiliated with Fudan University (Approval No. 2024K329). This randomized controlled trial (RCT) was registered with the World Health Organization's Primary Registry, the Chinese Clinical Trial Registry [ChiCTR2500095297]. Prior to participation, all patients were informed about the purpose of the study, and written informed consent was obtained from each participant.

Sample Size

Given the lack of prior studies in this area, the sample size for this study was estimated based on data from a preliminary pilot experiment. This randomized controlled trial utilized a parallel-group design, with the visual analogue scale (VAS) as the primary outcome measure-a continuous variable (the SF-MPQ total pain score demonstrated a strong positive correlation with the pain severity score assessed by the VAS ($r=0.753$, $P<0.001$)).[30] Sample size calculations were performed using G*Power 3.1.9.7 software. The significance level was set at $\alpha=0.05$ (two-sided), the effect size $d=0.80$, and statistical power was set at 90% ($1-\beta=0.90$). Based on these parameters, the minimum required sample size was calculated to be 34 participants per group ($N_1 = N_2 = 34$). Allowing for an anticipated dropout rate of 20%, at least 43 participants were required in each group.

Participants

A total of 91 participants were assessed for eligibility, and 86 patients with CP were ultimately recruited from the Department of Pain Management at Huadong Hospital, affiliated with Fudan University. All patients declined surgical intervention and provided written informed consent. The CONSORT flow diagram illustrating the RCT evaluating the efficacy of MT in patients with CP is presented in Figure 1.

Inclusion Criteria

1. Meeting the diagnostic criteria for CP:[31] 1. Experiencing persistent or recurrent pain for more than 3 months. 2. Aged between 18 and 70 years. 3. Pain has a significant impact on quality of life, sleep quality, or mood. 4. Abstinence from caffeine, alcohol, and medications that may affect HRV parameters for at least 24 hours prior to assessment, and not currently receiving any treatment. 5. Provision of written informed consent.

Exclusion Criteria

1. Presence of severe cardiovascular or cerebrovascular diseases, arrhythmias, hematological disorders, malignancies, or significant organ dysfunction. 2. Menstruation or pregnancy. 3. History of skin allergies or other serious dermatological conditions. 4. Presence of other neurological disorders. 5. Major psychiatric illness, cognitive impairment, or any condition that precludes cooperation with study procedures. 6. Refusal to provide written informed consent.

Additional Exclusion Criteria

1. Patients who received alternative treatment regimens or who withdrew during the treatment or follow-up period.
2. Occurrence of serious adverse events necessitating a change in treatment.

Randomization and Blinding

To ensure randomized group allocation, a random number table (RNT) was used to generate random numbers according to the study requirements. Participants were then ranked in ascending order based on these numbers and randomly assigned to groups in a 1:1 ratio. Specifically, the selected random numbers were divided into two groups based on their values: participants with smaller numbers were assigned to the experimental group (EG), while those with larger numbers were allocated to the control group (CG) The EG received both MT intervention and health education, while the CG received health education only To ensure the integrity of the data and minimize potential bias from participants or

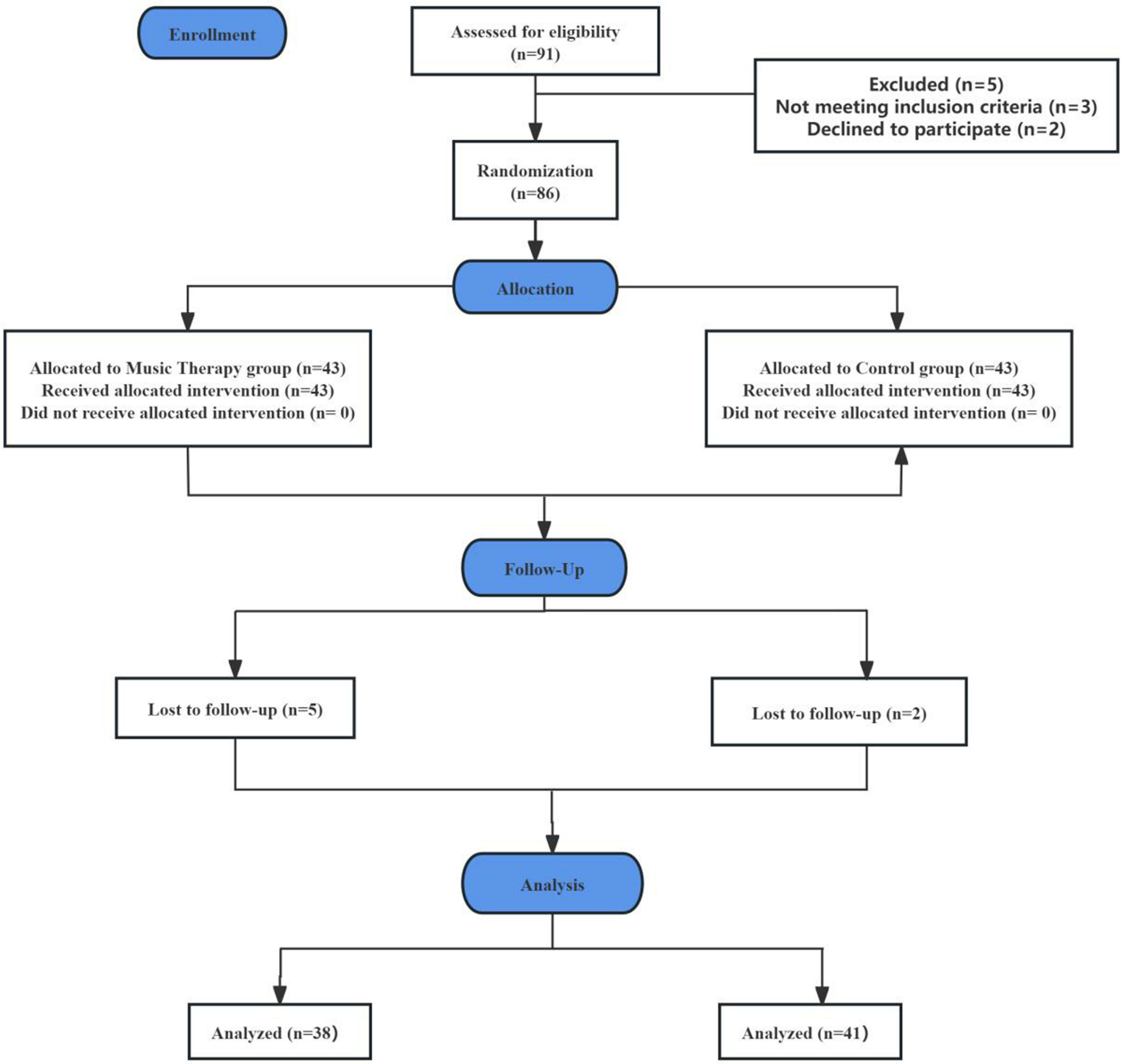

Figure 1 CONSORT flow chart for patient enrollment.

researchers, data collection was conducted by an independent researcher who was not involved in the study Additionally, the hypothesis and objectives of the study were concealed from both participants and data collectors throughout the trial. Furthermore, to further minimize potential bias, the independent researcher responsible for data collection maintained no direct contact with the principal investigator or the individual responsible for randomization. This approach was implemented to ensure the independence and objectivity of the data collection process.

Outcome Measures

To minimize measurement error, all assessments were conducted by a single designated evaluator. In the EG, patients completed the Short-Form McGill Pain Questionnaire (SF-MPQ), Patient Health Questionnaire-9 (PHQ-9), Generalized Anxiety Disorder-7 (GAD-7), Pittsburgh Sleep Quality Index (PSQI), and HRV measurements at three time points: before the intervention, immediately after the music listening session, and two weeks post-intervention In the CG, patients completed the SF-MPQ, PHQ-9, PSQI, and HRV assessments before the intervention and again two weeks later.

Primary Outcome Measures

The SF-MPQ, adapted from the original McGill Pain Questionnaire, evaluates both sensory and affective dimensions of pain through subjective reporting. The SF-MPQ comprises the Pain Rating Index (PRI), VAS, and Present Pain Intensity (PPI). The PRI is further divided into the Sensory Pain Rating Index (S-PRI; items 1–11) and the Affective Pain Rating Index (A-PRI; items 12–15), each graded on a scale from 0 (no pain) to 3 (severe pain), with a maximum total score of 45. Higher scores indicate greater pain severity. The VAS is scored from 0 (no pain) to 10, with ≤3 indicating mild pain, 4–6 moderate pain, and ≥7 severe pain. The PPI categorizes pain as none, mild, discomforting, distressing, horrible, or excruciating, corresponding to scores from 0 to 5.

Secondary Outcome Measures

The PHQ-9 and GAD-7 are validated instruments widely used for the assessment of depression and anxiety, respectively. The PHQ-9 consists of nine items with a total possible score of 27: mild depression (6–9), moderate (10–14), moderately severe (15–21), and severe (22–27). The GAD-7 includes seven items with a total score of 21: mild anxiety (6–9), moderate (10–14), and severe (15–21).

The PSQI was used to assess patients' sleep quality. The PSQI comprises seven components, each scored from 0 to 3, with higher total scores indicating poorer sleep quality.

HRV was analyzed using both time-domain and frequency-domain indices. The primary time-domain measure was the standard deviation of all normal sinus intervals (SDNN), which reflects overall HRV. Frequency-domain analysis included the following indices: 1. Total power (TP): Represents the overall ANS activity. 2. LF: Reflects combined sympathetic and parasympathetic (vagal) modulation of the sinoatrial node, with sympathetic tone as the dominant contributor. 3. HF: Indicates vagal (parasympathetic) activity. 4. Low frequency/high frequency (LF/HF) Ratio: The ratio of LF to HF power is widely recognized as an index of sympathovagal balance. An increased LF/HF ratio suggests heightened sympathetic excitability, while a decreased ratio indicates autonomic imbalance. 5. Very low frequency power (VLF): Although its physiological significance remains under investigation, VLF is thought to be associated with factors such as thermoregulation of peripheral vascular tone, renin-angiotensin system activity, blood volume fluctuations, cardiac pump function, and tidal volume variability. It should be noted that frequency-domain HRV indices often exhibit non-normal distributions; therefore, it is recommended to apply a natural logarithmic transformation to the results obtained through Fourier analysis (expressed as $\ln[\mathrm{ms}^2]$) for statistical evaluation.

Interventions

Experimental Group

Prior to the intervention, baseline information—including age, gender, height, weight, and pain duration—was collected from CP patients who met the inclusion criteria. Participants first completed a series of validated subjective questionnaires: the SF-MPQ, PHQ-9, GAD-7, and PSQI. Subsequently, HRV assessments were conducted in a quiet room to minimize external influences. HRV was measured using the ZSY-1 HRV detector (Shenyang Weijin Gene Technology Co., Ltd., China). To minimize the influence of diurnal variation, all measurements were performed between 08:00 and 12:00. The testing environment was controlled to maintain a quiet atmosphere, a constant room temperature of approximately 20°C, and stable lighting. Subjects were seated comfortably in a specialized chair and instructed to remain still and refrain from speaking or moving unless absolutely necessary. Each HRV recording lasted for 5 minutes. The data acquisition system employed Fourier transform analysis to generate both time-domain and frequency-domain measures, including TP, LF, HF, the LF/HF ratio, VLF, and SDNN. Immediately following baseline measurements, participants in the EG received an audio intervention at a frequency of 8–150 Hz The audio provided guidance for inhalation and exhalation, prompting participants to synchronize their breathing at a rate of 12 breaths per minute. After the intervention, HRV was reassessed under identical conditions. Upon completion of HRV measurements, health education was delivered by trained personnel.

Long-term Music Intervention: In addition to health education, patients were instructed to listen attentively to the music using noise-canceling headphones on their mobile phones after lunch, before dinner, and before falling asleep.

During each session, patients were advised to sit or lie down comfortably, close their eyes, relax their bodies, and adjust the volume to a comfortable level (between 55–70 dB). To minimize external distractions, patients were encouraged to avoid text messages, phone calls, and other potential interruptions, and to maintain a quiet environment in order to maximize comfort and the effectiveness of the intervention. Special attention was given to ensuring that, during each listening session, patients followed the audio prompts to maintain regular breathing patterns (eg., "breathe in-please inhale; breathe out-exhale") throughout the duration of the music. Each intervention session lasted 10 minutes and was performed three times daily. If patients felt comfortable, the session could be repeated once more as desired. The intervention was conducted seven days per week for a total duration of two weeks. Note: the MT interventions administered to the EG, comprising both immediate and long-term sessions, consisted of receptive MT.

We employed a standardized, soothing synthesized music track that integrated white noise and brainwave entrainment technology. The acoustic spectrum was calibrated to a frequency range of 8–150 Hz with a sound intensity of 50–70 dB. These specific parameters were selected based on physiological evidence regarding their therapeutic efficacy:

8–13 Hz (Alpha Band): Targeted to stimulate alpha brainwave activity, thereby promoting relaxation and mental calmness,[32] 16–150 Hz (Low-Frequency Acoustic Stimulation): Selected to facilitate pain relief and stress reduction, as well as to stabilize mood and promote sleep.[33] Sound Intensity (50–70 dB): Although 60–85 dB is generally considered the optimal range for human hearing,[34] we adjusted our protocol to 50–70 dB. This range adheres to Standley's recommendation that therapeutic music should exceed ambient noise levels by approximately 10 dB to ensure efficacy without causing disturbance.[35] Furthermore, noise-canceling headphones were used to deliver the intervention to minimize external distractions.

Supervision Protocol: Patients were instructed to promptly record their perceived pain intensity after each music listening session, as well as document the frequency and duration of daily sessions in a designated MT logbook, which was to be brought to follow-up visits. Weekly telephone calls were conducted to monitor patient adherence to the intervention schedule and to emphasize the importance of listening to music at the specified times. Family members were encouraged to participate in supervision to help ensure effective implementation of the intervention and to minimize noncompliance.

After two weeks, patients returned to the hospital for follow-up evaluations. HRV measurements and questionnaire assessments were repeated to observe changes in pain intensity, TP, LF, HF, LF/HF ratio, VLF, SDNN, as well as levels of anxiety, depression, and sleep quality.

Control Group

Prior to the intervention, baseline demographic and clinical data—including age, sex, height, weight, and pain duration—were collected from CP patients who met the inclusion criteria. Participants completed the same set of subjective questionnaires (SF-MPQ, PHQ-9, GAD-7, and PSQI) and underwent HRV assessment as described for the EG However, participants in the CG received only health education, without music intervention. The health education program consisted of providing patients with fundamental knowledge regarding CP, training them to use standardized assessment tools (eg., the VAS and pain diaries) to monitor pain intensity, and advising them to engage in moderate physical activity to mitigate pain symptoms. After two weeks, patients returned to the hospital for repeat HRV testing and questionnaire evaluations. The detailed study protocol is provided in the Supplementary Material.

Statistical Analysis

All statistical analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables that conformed to a normal distribution are presented as mean ± standard deviation (SD). The Kolmogorov–Smirnov (K-S) test \was used to assess the normality of data distributions. For normally distributed variables, independent sample *t*-tests were used for intergroup comparison, while paired sample t-tests were applied to evaluate within-group changes from baseline at each time point. For variables not conforming to a normal distribution, nonparametric tests were employed; specifically, the Mann–Whitney *U*-test was used for pairwise comparisons between groups. Categorical variables are expressed as frequencies and percentages, and intergroup comparisons were conducted using the chi-square test. A p-value < 0.05 was considered statistically significant.

Results

Baseline Characteristics

A total of 86 patients with CP were enrolled in the study. During the trial, 5 participants from the EG and 2 from the CG withdrew, resulting in 79 patients who completed the study Of these, 33 were male and 46 were female. There were no significant differences between the two groups with respect to demographic or clinical characteristics, including age, gender, height, weight, and heart rate ($p > 0.05$), indicating that the groups were comparable at baseline (see Table 1).

Comparison of SF-MPQ Scores During Treatment

After two weeks of treatment, both the EG and CG demonstrated statistically significant reductions in A-PRI, S-PRI, PRI, VAS, PPI, and overall SF-MPQ scores compared to baseline ($p < 005$). Notably, the PPI scores of patients in the EG were significantly lower than those in the CG ($p < 005$). Additionally, the results indicated that PPI scores in both groups gradually decreased as the duration of the intervention increased. At the end of the second week of treatment, the EG demonstrated a greater improvement in PPI scores compared to the CG Similarly, after two weeks of treatment, A-PRI, S-PRI, PRI, VAS, and total SF-MPQ scores were all lower than baseline in the EG, paralleling the trend observed in the CG However, there were no statistically significant differences between the groups in terms of A-PRI, S-PRI, PRI, VAS, or total SF-MPQ scores after treatment ($p > 0.05$). (see Table 2)

Table 1 Baseline Characteristics (n = 79, Mean ± SD)

Features	CG, n = 41	EG, n = 38	P value
Age (yrs), Mean (SD)	40.00±1.85	40.18±1.68	0.942
Sex (M/F), N	16/25	17/21	0.607
Height (cm), Mean (SD)	167.46±1.53	166.50±1.43	0.649
Heart Rate (b/m), Mean (SD)	83.76±2.20	88.95±2.20	0.100
Body weight (kg), Mean (SD)	64.41±1.98	64.05±1.94	0.896
BMI (kg/m^2), Mean (SD)	22.79±0.44	22.96±0.46	0.789
Duration of pain (months), Median [IQR]	46(8.50–54.00)	42(9.00–48.00)	0.881

Notes: Based on the results of the normality test, continuous variables are presented as mean ± SD or median [IQR], as appropriate. Gender, a categorical variable, is expressed as frequency (N). EG: experimental group (MT intervention plus health education); CG: control group (health education only).
Abbreviations: SD, standard deviation; BMI, body mass index; IQR, interquartile range.

Table 2 Comparison of SF-MPQ Scores During Treatment (n = 79, Mean ± SD)

Index	Peer Group	Pretreatment Baseline	Posttreatment
			14 Days
A-PRI (score)	CG (n = 41)	4.34±3.230	3.41±3.082*
	EG (n = 38)	5.11±3.109	2.87±2.612*
	95% CI	(−0.659, 2.186)	(−1.831, 0.739)
	T	1.069	−0.846
	P	0.288	0.400
S-PRI (score)	CG (n = 41)	7.02±5.174	5.39±4.759*
	EG (n = 38)	5.53±4.266	3.55±4.078*
	95% CI	(−3.632, 0.636)	(−0.155, 3.831)
	T	−1.398	1.836
	P	0.166	0.070

(*Continued*)

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Table 2 (Continued).

Index	**Peer Group**	**Pretreatment Baseline**	**Posttreatment**
			14 Days
PRI (score)	CG (n = 41)	11.37±7.412	8.80±6.904*
	EG (n = 38)	10.63±6.331	6.42±5.411*
	95% CI	(−3.834, 2.366)	(−0.410, 5.178)
	T	−0.472	1.699
	P	0.639	0.093
VAS (score)	CG (n = 41)	5.88±2.100	4.54±1.989*
	EG (n = 38)	5.71±2.415	3.71±1.784*
	95% CI	(−1.179, 0.844)	(−1.675, 0.023)
	T	−0.330	−1.938
	P	0.743	0.055
PPI (score)	CG (n = 41)	2.61±1.115	2.29±1.055*
	EG (n = 38)	2.26±0.950	1.58±0.858*
	95% CI	(−0.812, 0.119)	(−1.147, −0.281)
	T	−1.481	−3.284
	P	0.143	0.002
SF-MPQ (score)	CG (n = 41)	19.85±9.430	15.63±9.159*
	EG (n = 38)	18.61±8.126	12.16±7.050*
	95% CI	(−5.207, 2.710)	(−0.207, 7.159)
	T	−0.628	1.880
	P	0.532	0.064

Notes: *Represents $p < 0.05$ compared with before treatment.

Comparison of PHQ-9, GAD-7, and PSQI Scores During Treatment

After two weeks of treatment, both the EG and CG exhibited significant reductions in GAD-7, PHQ-9, and PSQI scores compared to baseline ($p < 005$). The decrease in PHQ-9 scores was significantly greater in the EG than in the CG ($p < 005$), indicating a more pronounced improvement in depressive symptoms among patients receiving MT. By the end of the second week, the EG demonstrated superior improvement in PHQ-9 scores relative to the CG Although GAD-7 and PSQI scores were also reduced in both groups after two weeks, consistent with improvements in anxiety and sleep quality, no statistically significant differences were observed between the groups for these measures after treatment ($p > 0.05$). (see Table 3)

Table 3 Comparison of PHQ-9, GAD-7 and PSQI Scores During Treatment (n = 79, Mean ± SD)

Index	**Peer group**	**Pretreatment Baseline**	**Posttreatment**
			14 Days
PHQ-9 (score)	CG (n = 41)	10.07±7.421	8.63±6.792*
	EG (n = 38)	10.05±6.358	5.89±4.985*
	95% CI	(−3.128, 3.087)	(0.081, 5.398)
	T	−0.013	2.054
	P	0.990	0.044
GAD-7 (score)	CG (n = 41)	10.15±7.034	8.29±6.724*
	EG (n = 38)	9.55±6.761	6.34±6.406*
	95% CI	(−3.690, 2.502)	(−0.997, 4.898)
	T	−0.382	1.318
	P	0.704	0.091

(*Continued*)

Table 3 (Continued).

Index	Peer group	Pretreatment Baseline	Posttreatment
			14 Days
PSQI (score)	CG (n = 41)	8.66±5.379	8.05±5.399*
	EG (n = 38)	9.82±4.585	7.95±4.538*
	95% CI	(−1.090, 3.405)	(−2.345, 2.142)
	T	1.025	−0.090
	P	0.308	0.929

Notes: *Represents $p < 0.05$ compared with before treatment.

Comparison of HRV Changes During Treatment

After two weeks of treatment, the LF/HF ratio in the EG was significantly lower than at baseline ($p < 005$) and showed a greater decrease compared to the CG ($p < 0.05$). This suggests that MT was more effective in improving autonomic balance as reflected by the LF/HF ratio. No significant differences were observed between the groups in TP, LF, HF, VLF, or SDNN following treatment ($p > 0.05$). Immediately after listening to music, EG patients exhibited significant increases in both LF and HF compared to pre-intervention values ($p < 005$), while there were no significant changes in VLF, LF/HF, TP and SDNN immediately following music intervention ($p > 0.05$). After two weeks of MT treatment, patients in the EG exhibited changes in VLF, HF, LF/HF, and TP levels However, there were no statistically significant differences in LF and SDNN before and after the two-week MT intervention ($p > 0.05$). In addition, the LF/HF ratio in the EG was significantly lower after two weeks of MT compared to immediately following MT ($p < 005$), indicating that long-term MT was more effective in improving LF/HF than immediate MT (see Table 4).

Table 4 Comparison of HRV Changes During Treatment (n = 79, Mean ± SD)

Index	Peer group	Pretreatment Baseline	Posttreatment
			14 days
TP [ln(ms^2)]	CG (n = 41)	6.71±0.63	6.55±0.91
	EG (n = 38)	6.34±1.01	6.73±1.09*
	95% CI	(−0.746, 0.020)	(−0.274,0.624)
	T	−1.927	0.777
	P	0.058	0.439
LF [ln(ms^2]	CG (n = 41)	5.43±0.81	5.37±0.945
	EG (n = 38)	5.11±1.22	5.35±1.141$^{\#}$
	95% CI	(−0.782, 0.156)	(−0.487, 0.450)
	T	−1.332	−0.080
	P	0.187	0.937
HF [ln(ms^2)]	CG (n = 41)	4.46±1.26	4.48±1.23
	EG (n = 38)	3.94±1.24	4.74±1.00$^{*\#\&}$
	95% CI	(−1.080, 0.421)	(−0.251, 0.758)
	T	−1.842	1.002
	P	0.069	0.319
LF/HF	CG (n = 41)	0.79±1.03	0.88±0.78
	EG (n = 38)	1.17±0.96	0.55±0.66$^{*\&}$
	95% CI	(−0.731, 0.823)	(−0.653, −0.003)
	T	1.666	−2.011
	P	0.100	0.048

(*Continued*)

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Table 4 (Continued).

Index	**Peer group**	**Pretreatment** **Baseline**	**Posttreatment**
			14 days
VLF [ln(ms^2)]	CG (n = 41)	5.86±0.64	5.72±0.96
	EG (n = 38)	5.53±1.07	5.96±1.21*
	95% CI	(−0.731, 0.068)	(−0.238, 0.735)
	T	−1.662	1.017
	P	0.102	0.312
SDNN (ms)	CG (n = 41)	38.26±44.40	30.59±16.01
	EG (n = 38)	27.84±14.48	37.14±34.43*
	95% CI	(−25.455, 4.625)	(−5.342, 18.434)
	T	−1.379	1.096
	P	0.172	0.276

Notes: *Represents that after listening to music for two weeks, p <0.05 compared with before treatment; # indicates that immediately after listening to music, p <0.05 compared with before treatment; & indicates that immediately after listening to music, p <0.05 compared with after listening to music for two weeks.

Discussion

The Relationship Between CP and Autonomic Nervous Function

Pain serves as a protective mechanism that signals the need for prompt and appropriate action to prevent or minimize injury. Increasing evidence suggests that MT-based interventions are safe, effective, and non-invasive modalities that can be clinically applied to manage various pain-related conditions. MT has been shown to reduce patients' perception of pain, thereby improving overall quality of life.[15,36] In this study, we found that MT effectively alleviates pain in patients with CP. A two-week MT intervention in the EG significantly improved S-PRI, PRI, PPI, and SF-MPQ scores compared to the CG (p < 005). Notably, the PPI score in the EG was markedly reduced following the two-week MT intervention, indicating a decrease in immediate pain intensity among CP patients These findings suggest that MT is an effective intervention for significantly alleviating pain intensity perception in patients with CP. These findings are consistent with results from multiple randomized controlled trials investigating the analgesic effects of MT,[37–40] reflecting that music intervention has a notable analgesic effect and can provide meaningful relief from pain.

The mechanisms by which MT alleviates pain can be interpreted through several theoretical frameworks, including the cognitive-behavioral model, gate control theory, and neuroendocrine mechanisms. According to the cognitive-behavioral model, music enhances individuals' sense of autonomy, serves as a distraction, and thereby reduces the subjective experience of pain.[41] Gate control theory posits that synapses transmitting signals from peripheral nerve receptors to the brain's gray matter act as key "gates" in the process of pain conduction. MT can modulate these gates, effectively "closing" them and thereby reducing the transmission and perception of pain stimuli.[42] The neuroendocrine theory suggests that music influences the secretion of endogenous endorphins and catecholamines, which in turn helps to reduce pain perception in individuals.[43]

In this study, we also found no significant differences between the EG and the CG in VAS or A-PRI scores two weeks after MT (p > 005). This may be attributed to the transient nature of music-induced analgesia, limitations in pain-related distraction, insufficient patient engagement, or reduced absorption in the intervention.[21] This phenomenon is closely associated with the analgesic mechanisms mediated by the descending pain modulatory system (DPMS).[44] The DPMS is a "top-down" pathway involved in endogenous pain modulation, transmitting signals from the brain to the brainstem.[45] It regulates incoming nociceptive signals bidirectionally through the coordinated activity of multiple brain regions and neurotransmitters. The core mechanism involves inhibition of pain signal transmission at the spinal cord level via descending pathways, thereby modulating overall pain perception.[46] In addition, the activity of the DPMS is influenced by factors such as attention, emotion, and individual pain sensitivity, which may interfere with the sustained analgesic effects of music intervention.[47] In addition, the analgesic effect of music is influenced by the type of music used.

Numerous studies have demonstrated that self-selected or personally preferred music produces a stronger analgesic effect compared to music chosen by researchers.[48–50] Playing patients' preferred music can activate memory, associative, and emotional regions within their cognitive system. This activation helps to divert the patient's attention away from the source of pain by providing more salient external stimuli.[51] Although studies have confirmed that MT can modulate pain, its precise mechanisms of action in patients with CP remain unclear. Therefore, further research is needed to elucidate the relationship between MT and CP, and to uncover the underlying mechanisms through which MT exerts its effects in this population.

The Relationship Between Music, Anxiety, and Depression

In this study, patients in the EG received MT for two weeks Compared to the CG, EG patients showed a significantly greater reduction in PHQ-9 scores ($p < 005$). These findings indicate that MT not only alleviates pain in patients with CP, but also effectively reduces depressive symptoms, thereby exerting a positive psychological impact on pain-related outcomes.

Depression is a prevalent mental disorder that arises from the complex interplay of social, psychological, and biological factors.[52] Although psychotherapy and pharmacological treatments can be effective for depression, prolonged use of medication may result in drug dependence as well as mental and cognitive impairment.[53] Numerous clinical studies have demonstrated that listening to music has a beneficial effect on depressive symptoms, regardless of whether it is used alone or in combination with other standard treatments.[54] This effect is primarily attributed to music's ability to activate multiple brain regions involved in emotional processing and regulation, including the insular cortex, cingulate cortex, amygdala, and hypothalamus.[55,56] As a result, music can promote the release of β-endorphin and dopamine while reducing the release of nitric oxide, thereby inducing pleasant emotional states and suppressing central nervous system excitability. These processes contribute to both analgesic effects and the alleviation of negative emotions, such as depression, in patients.[57] Among these neurotransmitters, 5-hydroxytryptamine (5-HT), also known as serotonin, plays a crucial role in the central nervous system and is closely associated with the regulation of emotions, sleep, and appetite.[58] Research has shown that depletion of 5-HT can result in impaired emotional regulation, which in turn contributes to the development of depressive symptoms.[59] It has been demonstrated that MT can significantly increase serum 5-HT levels in patients with depression, thereby alleviating depressive symptoms.[54] In addition, dysfunction of the hypothalamic-pituitary-adrenal (HPA) axis plays a significant role in the onset and progression of depression. Music stimulates multiple sensory pathways, which can protect the HPA axis from dysfunction, inhibit corticosterone secretion, upregulate the expression of brain-derived neurotrophic factor (BDNF), and promote synaptic health and neuronal growth. Collectively, these effects contribute to the alleviation of depressive symptoms.[60,61] However, in this study, no significant difference in anxiety levels was observed between the EG and the CG after two weeks of MT ($p > 005$). This finding is consistent with previous clinical research indicating that MT is often less effective at simultaneously alleviating both depression and anxiety symptoms in most patients with CP.[62] This discrepancy may be attributed to the distinct neurobiological mechanisms involved. MT is believed to alleviate depressive symptoms primarily by activating the limbic system, regulating the dopaminergic reward system, and promoting endorphin release. In contrast, the pathophysiology of anxiety is predominantly driven by the locus coeruleus, which activates the amygdala via norepinephrine release to trigger emotional and somatic anxiety responses.[63] Current music intervention models (eg., passive listening or patient-selected music) may not adequately target these anxiety-specific neural pathways, thereby limiting their efficacy in managing anxiety.

Therefore, the underlying mechanisms of MT in the management of CP warrant further investigation to better address the associated comorbidities. In summary, our study demonstrates that long-term MT not only alleviates CP but also improves pain-related depression in affected patients.

The Relationship Between Music and Sleep

In this study, after two weeks of MT in the EG, no significant difference in PSQI scores was observed between the EG and CG ($p > 005$). Although numerous studies have reported that music can promote relaxation and improve sleep, our findings suggest that MT alone has no significant effect on sleep disturbances in patients with CP. This discrepancy may be attributed to the reliance on self-reported measures for assessing sleep quality, which are susceptible to various confounding factors. As noted by Chang et al[64] numerous studies have sought to validate the efficacy of music in improving sleep quality. However, the limited number of randomized controlled trials hinders a comprehensive and robust validation of these effects. Furthermore, existing studies are often limited by methodological shortcomings and a reliance on subjective self-report measures. Notably, when objective methods (eg., polysomnography) are employed to evaluate music interventions, the findings frequently diverge from those obtained via subjective assessments.[65] Additionally, many clinical studies evaluating the impact of music therapy on sleep disorders often combine MT with other interventions, making it difficult to isolate the effects of MT alone.[66] In addition, in our study, MT was administered to CP patients for a duration of two weeks. This relatively short intervention period may not adequately reflect the long-term effects of MT, and any observed improvements in sleep quality may be only temporary. A meta-analysis has shown that MT lasting more than four weeks produces significantly greater improvements in sleep quality compared to interventions of less than four weeks.[67]

Patients with CP frequently experience comorbid sleep disturbances, which are characterized by prolonged sleep onset latency, increased frequency of nighttime awakenings, reduced total sleep duration, diminished restorative quality upon awakening, and decreased overall sleep efficiency.[68] These symptoms indicate that individuals with CP commonly experience sleep disorders, such as difficulty falling asleep and insufficient effective sleep duration. Studies have shown that approximately 50% of patients with CP suffer from sleep disturbances. Conversely, about 50% of individuals with insomnia also report CP.[69] These findings demonstrate a bidirectional relationship between CP and sleep disturbances. Research has shown that disrupted sleep can inhibit the biological activity of endogenous opioids, reduce the expression of opioid receptors in the central nervous system, and diminish the binding affinity of μ- and δ-opioid receptors to their ligands. Consequently, these changes weaken the analgesic effects mediated by endogenous opioids in the body.[68,70] In addition, CP patients with sleep disorders tend to exhibit more severe depressive symptoms, greater functional impairment, and a reduced quality of life.[71] These findings underscore the importance of alleviating sleep disturbances in individuals with CP. Therefore, future research should further explore the mechanisms by which MT may improve sleep disorders, in order to develop more effective treatment options for complications associated with CP.

The Relationship Between Pain and HRV

Compared to other pain assessment indicators, HRV offers an objective and quantitative method for evaluating pain, thereby minimizing the influence of subjective factors.[72] In addition, HRV demonstrates high sensitivity in detecting subtle changes in ANS activity related to stress. This suggests that HRV may effectively reflect variations in anxiety and depression levels associated with pain.[73] Therefore, HRV is generally considered a valuable indicator for the assessment of pain. In this study, after two weeks of MT in the EG, there was a significant difference in the LF/HF ratio between the EG and the CG (p < 005) The LF/HF ratio in the EG showed a significant decrease following treatment However, no significant differences were observed between the groups in other HRV parameters, including LF, HF, VLF, SDNN, and TP ($p > 0.05$).

CP is a persistent pain stimulus that gradually disrupts both physiological and emotional balance. It activates the body's stress response and heightens autonomic nervous system activity in reaction to pain. Over time, this sustained activation can lead to an overall decline in HRV function.[74] In this study, the LF/HF ratio in the EG was significantly reduced after MT compared to the CG This finding suggests that MT suppresses sympathetic nervous system activity and helps regulate the balance between sympathetic and parasympathetic nervous system function. Masel et al[75] reported a decrease in the logarithmic LF/HF ratio, indicating an improved balance between sympathetic and parasympathetic activity. Furthermore, the LF/HF ratio was found to be positively correlated with the Numeric Rating Scale (NRS) score, a widely accepted instrument for assessing both acute and CP. Therefore, the reduction in LF/HF ratio observed in this study suggests that MT effectively alleviated pain levels in patients with CP to some extent. Furthermore, numerous studies have demonstrated that ANS activity, as assessed by HRV parameters, is closely associated with anxiety and depression. In particular, an increased LF/HF ratio has been linked to major depressive disorder.[76] Therefore, the decrease in LF/HF ratio observed in this study indicates that MT may improve depressive symptoms in patients with CP, which is consistent with the reduction in PHQ-9 scores observed in the EG However, no significant differences were found in other HRV parameters (such as HF and LF) between the EG and CG following MT. This may be due to the fact that HF values are particularly susceptible to influences from heart rate, respiratory rate, and other confounding factors.[77,78] Studies have suggested that, during HRV assessment, the patient's respiratory rate should be maintained within a range of 9–24 breaths per minute (0.15–0.4 Hz) to ensure optimal measurement accuracy.[79] In this study, the respiratory rate of CP patients was not controlled during HRV assessment, which may be a primary reason for the lack of significant differences in HF between the two groups. Additionally, a reduction in LF power–reflecting decreased sympathetic excitability and enhanced parasympathetic tone–has been associated with analgesic effects across various pain conditions. However, in the present study, we observed no significant differences in LF levels between the experimental and control groups. This may be attributed to the insufficient duration of the intervention. Specifically, a two-week course of music therapy may not be long enough to significantly lower baseline LF levels in patients with chronic pain, a finding that is consistent with the results reported by Muthulingam et al[80] In summary, MT can improve the LF/HF balance in patients with CP and clinically, this intervention may serve as an effective strategy to alleviate pain intensity. However, its effects on other HRV parameters, such as HF, LF, SDNN, TP, and VLF, remain unclear. Additionally, as pain is a subjective experience, there is currently a lack of objective assessment methods for evaluating pain in clinical practice. In this experiment, HRV was utilized as a method to assess ANS function and its adaptation to various physiological and pathological states, thereby contributing to a more objective evaluation of pain. Future research should further explore the potential of HRV as an objective and quantitative tool for assessing the efficacy of MT in alleviating pain in patients with CP.

Innovation and Limitations

The main innovations of this study are as follows: 1. We implemented a comprehensive framework to evaluate both the immediate and long-term effects of MT on patients with CP. This included a multidimensional assessment of pain, anxiety, depression, and sleep quality using validated scales to establish the safety and efficacy of MT. 2. By integrating HRV analysis, this study provides objective physiological evidence regarding the ANS response to MT, bridging the gap between subjective self-reports and physiological mechanisms.

However, this study also has several limitations: 1. Given that the follow-up was limited to two weeks, the long-term clinical efficacy of MT remains uncertain and warrants further longitudinal investigation. 2. CP encompasses a wide range of conditions, and this study did not focus on a single disease entity, which may limit the specificity of its findings. 3. This study employed only a single treatment protocol, and the optimal frequency and duration of MT remain undetermined. Further research is needed to explore the most effective dosage, parameters, and course of MT. Moreover, although guided breathing was employed during HRV assessment, the respiratory rate was not strictly controlled, which may introduce a significant confounding factor. Consequently, future studies should standardize respiratory frequency and incorporate concurrent respiratory monitoring to enhance the methodological rigor of HRV evaluation. 4. Although MT has been shown to be an effective non-pharmacological approach for short- and medium-term pain relief, its long-term efficacy warrants further investigation. In the future, further research is needed to investigate the long-term clinical effects of MT using various approaches, such as improvisation and re-creation. 5. Corrections for multiple comparisons were not applied to the secondary outcome measures, which may increase the risk of Type I errors.

Conclusion

Listening to music may potentially reduce pain levels in patients with CP. However, while there was a trend toward improvement, it was not statistically superior to the CG for overall pain. Research has also observed that music may help alleviate depressive symptoms-a common disabling complication in chronic pain. Additionally, it may regulate the activity of the sympathetic and parasympathetic nervous systems in CP patients, potentially serving as a supplementary approach to managing their condition. However, the two-week music intervention did not significantly improve anxiety or sleep outcomes in patients with CP. This finding may be attributed to cognitive inertia, whereby subjective experiences remain anchored in prior negative cognitions despite positive changes in the patients' biological state.[81] Therefore, these findings require further validation through larger-scale, long-term studies.

Abbreviations

CP, Chronic pain; MT, Music therapy; EG, Experimental group; CG, Control group; SF-MPQ, Simplified mcGill pain questionnaire; PHQ9, Patient health questionnaire-9; GAD-7, Generalized anxiety disorder-7; PSQI, Pittsburgh sleep quality index; HRV, Heart rate variability; LF/HF, Low frequency/high frequency; NSAIDs, Non-steroidal anti-inflammatory drugs; ANS, Autonomic nervous system; RCT, Randomized controlled trial; RNT, Random number table; PRI, Pain rating index; VAS, Visual analogue scale; PPI, Present pain intensity; S-PRI, Sensory pain rating index; A-PRI, Affective pain rating index; TP, Total power; VLF, Very low frequency; SDNN, Standard deviation of all normal sinus intervals; DPMS, Descending pain modulatory system; 5-HT, 5-hydroxytryptamine; HPA, Hypothalamic-pituitary-adrenal; BDNF, Brain-derived neurotrophic factor; NRS, Numeric rating scale.

Data Sharing Statement

The datasets generated and analyzed during the current study are available from the corresponding author (Yongjun Zheng, PhD) upon reasonable request.

Ethics Approval and Consent to Participate

The study was conducted according to the principles of the Helsinki Declaration and approved by the Ethics Committee of Huadong Hospital Affiliated to Fudan University: No. 2024K32. This randomized controlled trial (RCT) has been registered at the Primary Registry of International Clinical Trial Registry Platform World Health Organization "Chinese Clinical Trial Registry" [ChiCTR2500095297]. All participants signed the informed consent form.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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