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Effects of music therapy on anxiety in patients with cancer: study protocol of a randomised controlled trial

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ABSTRACT

Introduction Although music therapy (MT) has been found to reduce anxiety in patients with cancer and delay tumour progression to some extent, its mechanism of action has not been determined. MT may reduce anxiety by reducing the concentrations of proinflammatory cytokines. The present study was designed to evaluate the effects of MT on anxiety and cytokine levels in patients with cancer.

Methods and analysis This randomised, open, single-centre parallel-controlled trial will randomise 60 patients with malignant tumours who meet the inclusion criteria in a 1:1 ratio to either an MT group or a non-MT (NMT) group. Patients in the MT group will receive emotional nursing care and individualised receptive MT for 1 week, whereas patients in the NMT group will receive emotional nursing care alone. Primary outcomes will include scores on the State-Trait Anxiety Inventory, Distress Thermometer and Hamilton Anxiety Scale. Secondary outcomes will include scores on the Quality of Life Questionnaire C30, serum concentrations of the cytokines interleukin (IL)-1β, tumour necrosis factor-α, IL-2R, IL-4, IL-6, IL-8 and IL-10, serum concentrations of the neurotransmitters 5-hydroxytryptamine, dopamine, norepinephrine, adrenocorticotropic hormone and γ-aminobutyric acid, and determination of gut microbiota populations.

Ethics and dissemination On 5 August 2020, the study protocol was approved by the Research Ethics Committee of the Yueyang Hospital of Integrated Traditional Chinese and Western Medicine of the Shanghai University of Traditional Chinese Medicine. The findings of this study will be published in peer-reviewed publications and presented at appropriate conferences.

Trial registration number CTR2000035244.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ All interventions will be instructor directed, with music therapists playing personalised music clips based on each patient's type of preferred music.

⇒ The study will evaluate cytokine levels, gut microbiota and neurotransmitters to explore the clinical evaluation of the efficacy of music therapy.

⇒ One limitation of this study will be its inclusion of patients from a single hospital, which may limit the generalisability of the study results.

⇒ A second limitation may be that the 1-week duration of music therapy may be regarded as too short.

INTRODUCTION

Current cancer treatments include surgical resection, chemotherapy, targeted therapy and immunotherapy. These treatments, as well as the disease itself, may have adverse psychological effects on patients, including psychological stress reactions and negative emotions such as anxiety and depression, negatively affecting patient quality of life.[1 2] A cross-sectional, prospective study suggested that the prevalence of moderate to severe depression in patients with advanced solid tumours was 29.2%.[3] The National Comprehensive Cancer Network has classified psychological problems in patients with cancer, such as anxiety and depression, as 'psychosocial distress'.[4] These psychological problems can interfere with patients' ability to cope with disease and have a negative impact on physical symptoms.[4] Reducing anxiety in patients with cancer may therefore have positive effects on their physical and mental health.

Current treatment of cancer-associated anxiety is frequently focused on the primary tumour. Few studies to date have focused on treating anxiety disorders caused by cancer, with even fewer focusing on non-pharmacological treatments. Music therapy (MT) has been defined by the American Music Therapy Association as the 'clinical and evidence-based use of music interventions to accomplish individualized goals within a therapeutic relationship by a credentialed professional who has completed an approved music therapy program'.[5] MT includes active methods, such as singing or playing instruments, and receptive methods, which involve the playing of prerecorded music under the guidance of a certified music therapist.[6] Over the last few decades, MT has evolved from a specialised field to a method of treating a wide range of conditions,[7] including perioperative cancer-associated anxiety[8] and anxiety

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in patients with breast[9] and lung[10] cancer. Evidence has shown that MT could help patients improve their positive attitude toward the disease by regulating their emotions and managing their symptoms.[11 12] Notably, the Clinical Practice Guidelines on the Evidence-Based Use of Integrative Therapies During and After Breast Cancer Treatment have recommended the application of MT to improve the quality of life and physical functioning of patients with breast cancer.[13]

The pathophysiological basis of anxiety disorders has not been determined yet, although structural brain abnormalities, neurobiochemical abnormalities and genetic factors are thought to be involved.[14] The primary mechanisms of concomitant anxiety and depression in patients with tumour are thought to involve an overactive hypothalamic–pituitary–adrenal (HPA) axis, inflammatory mediators and immune factors.[15 16] Patients with cancer were found more likely to develop depressive symptoms and had a poorer prognosis than healthy individuals. The development and treatment of cancers have been found to increase inflammation medicated by proinflammatory cytokines, such as interleukin (IL)-1, IL-6 and tumour necrosis factor (TNF)-α. This, in turn, resulted in dysregulation of the HPA axis and led to depression-like behaviours. Conversely, depression was shown to activate the HPA axis, resulting in the release of endogenous glucocorticoids, which caused depressive symptoms in patients with cancer.[17] The microbiome–gut–brain axis theory has suggested alternative pathways for the pathogenesis of tumour anxiety, especially anxiety associated with intestinal cancers. The intestinal flora were shown to regulate brain function via neural pathways involving the enteric and vagus nerves; endocrine pathways involving intestinal hormones; and immune pathways involving immune cells and cytokines,[18] thereby affecting mood, behaviour and neuroinflammation.[19] Many gut microbiota, including *Candida*, *Streptococcus*, *Enterococcus* and *Bacillus* spp and *Escherichia coli*, have been shown to produce neurotransmitters, such as 5-hydroxytryptamine (5-HT).[20 21]

In addition to directly influencing tumour development by regulating angiogenesis and the tumour growth microenvironment, chronic stress can indirectly affect tumour development by altering human hormone levels.[22] MT may affect tumour related anxiety by altering neuroendocrine factors and factors associated with the cellular immune system and the gut–brain axis. For example, music was shown to modulate salivary stress markers and physiological markers of the HPA axis[23] and to reduce depressive symptoms.[24] Exposure of mice to music was found to alter the expression of brain-derived neurotrophic factor (BDNF) in the hypothalamus.[25] BDNF has been associated with tumour development,[26 27] with high levels of BDNF expression in cancer indicating poor prognosis.[28 29] In depressed mice, MT increased serum 5-HT levels, decreased monoamine oxidase levels in hippocampal tissue and malondialdehyde levels in liver tissue, and relieved depression.[30] Improved mood has been shown to reduce anxiety and depression by influencing

metabolism and ultimately inhibiting tumour development.[31] However, despite evidence showing that MT can reduce anxiety in oncology patients and delay tumour progression to some extent, its exact mechanism of action is still unknown.

The present study will evaluate the effects on anxiety of patients with cancer of receptive and individualised MT under the guidance of a music therapist. This randomised controlled study will assess the ability of individualised MT to reduce cancer-related anxiety by analysing anxiety-related scales after MT. In addition, this study will evaluate cytokine levels, gut microbiota and neurotransmitters to explore the clinical evaluation of the efficacy of MT.

MATERIALS AND METHODS
Study design
This randomised controlled trial (RCT) will enrol 60 patients with cancer who are experiencing cancer-related anxiety. Patients will be randomly divided 1:1 into two groups, with patients in the MT group receiving emotional nursing care and individualised receptive MT (MT group) and patients in the non-MT group receiving emotional nursing care alone (NMT group) for 1 week. The study will be performed at Yueyang Hospital of Integrated Traditional Chinese and Western Medicine, Shanghai University of Traditional Chinese Medicine, between 10 December 2022 and 31 December 2023. Figure 1 shows the design of the trial based on standard protocol items. The Standard Protocol Items: Recommendations for Interventional Trials checklist is shown in online supplemental appendix 1.

Inclusion criteria
Subjects will be included if they (1) have a malignant tumour, as confirmed by histopathology or cytology; (2) have been treated for cancer-related anxiety or cancer itself for ≥2 months and ≤1 year; (3) meet the standard criteria for anxiety, including Hamilton Anxiety Scale (HAMA) scores ≥7 and ≤28 and State-Trait Anxiety Inventory (STAI) sores ≥20 and ≤80; (4) are aged 18–74 years, with no gender restrictions; (5) do not smoke or drink; (6) do not have psychiatric symptoms; (7) hear normally, and do not have a professional music background; (8) have normal heart, liver, kidney and blood test results, with all other vital signs being normal; (9) have not taken anti-anxiety medications within 4 weeks prior to study entry; (10) have an expected survival time >6 months and (11) provide written informed consent to study participation.

Exclusion criteria
Subjects will be excluded if they (1) are currently participating in other clinical studies or clinical trials; (2) have other serious diseases, such as infection, liver or kidney failure, making them unable, in the opinion of the project leader or researchers, to tolerate the treatment regimen of this study; (3) have primary or metastatic brain tumour, as confirmed clinically or radiologically; (4) are pregnant or
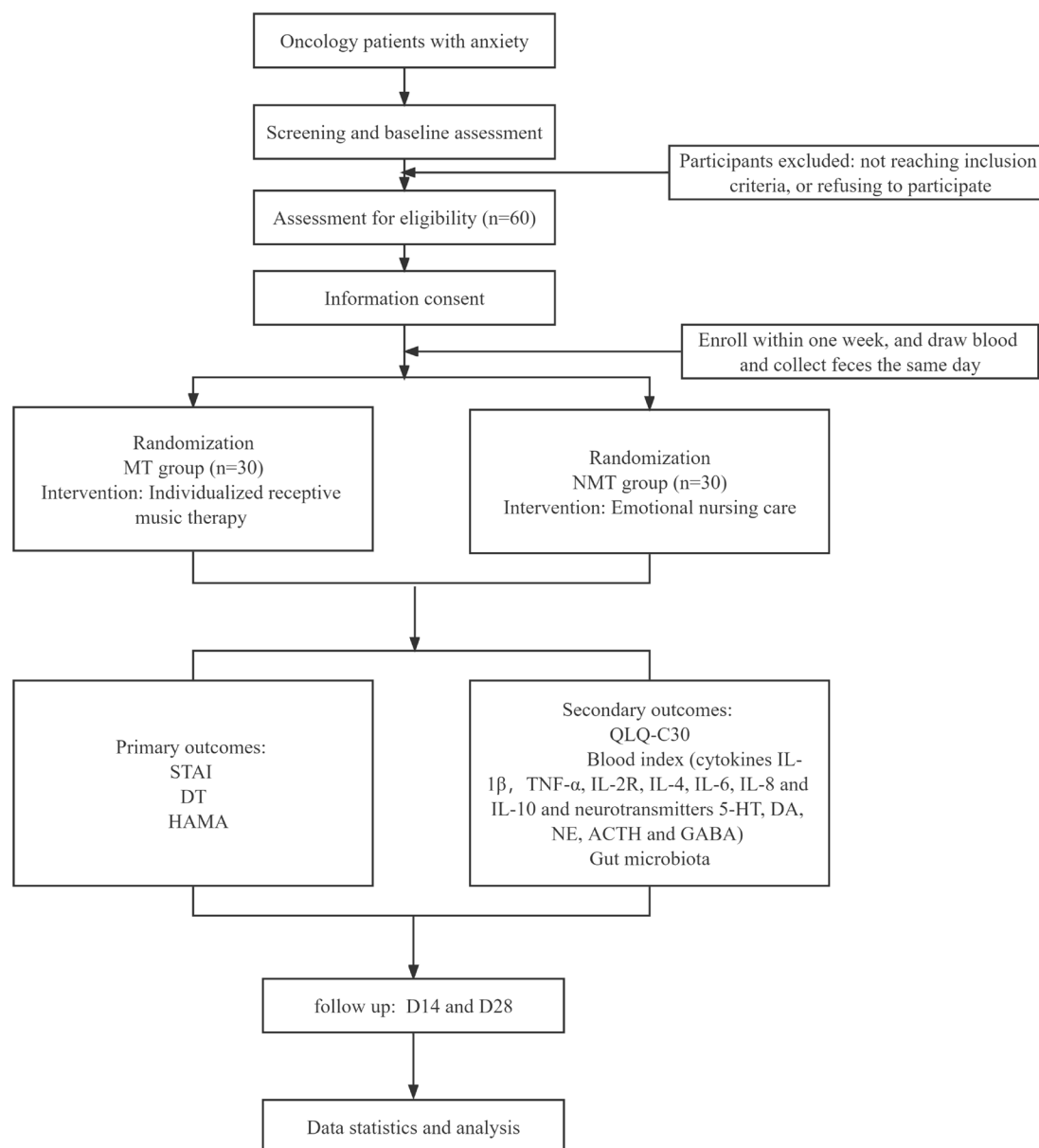
Figure 1 Flow chart of the trial design, based on standard protocol items. 5-HT, 5-hydroxytryptamine, ACTH, adrenocorticotropic hormone; DA, dopamine; DT, Distress Thermometer; HAMA, Hamilton Anxiety Scale; IL, interleukin; MT, music therapy; NE, norepinephrine; NMT, non-music therapy; QLQ-C30, Quality of Life Questionnaire C30; STAI, State-Trait Anxiety Inventory; TNF-α, tumour necrosis factor-α.

lactating women; (5) have received MT within 3 months prior to the study; (6) are taking anxiety medications or medications that can affect anxiety.

Rejection, suspension and shedding criteria
Patients will be discontinued from the study if they (1) are found not to meet the above inclusion criteria or meet the exclusion criteria; (2) show poor compliance or fail to follow up as required; (3) have incomplete medical records; (4) withdraw voluntarily from the study; (5) are regarded as unsuitable to continue the study due to serious deterioration of disease, severe complications or special physiological changes; or (6) are regarded by the investigator as unsuitable to continue the study. In

addition, patients in the control group will be discontinued if they listen to music during the study period.

Participant recruitment
This study aims to include 60 patients with cancer who are experiencing cancer-related anxiety. Patients at the Yueyang Hospital of Integrated Traditional Chinese and Western Medicine, Shanghai University of Traditional Chinese Medicine will be recruited by posting advertisements on the hospital's website and on posters. These advertisements will include brief descriptions of the study aims, requirements and methods. All participants will provide written informed consent. Patients will be recruited from December 2022 to December 2023.

Informed consent

All study processes will be explained to participants prior to the start of the study. Participants will also be informed that their participation in this trial is entirely voluntary and that they can opt out at any time. Each participant will be required to sign a written informed consent form before receiving any intervention. The informed consent is shown inonline supplemental appendix 2.

Randomisation and concealment of allocation

Patients will be randomly assigned to the treatment and control groups in a 1:1 ratio at the time of enrolment. A set of randomised numbers will be generated by SPSS V.22.0 software, with each number randomised into opaque envelopes. The order in which patients enter the study will be determined by the grouping of the corresponding envelopes allocated by the researcher.

Intervention

Patients in the NMT group will receive emotional nursing care but not be allowed to receive any treatment for anxiety or music listening. Emotional nursing care includes symptoms inquiry and timely communication when emotional distress occurs. Inquiry and communication will be carried out while the MT group performs the treatment. If treatment is required due to worsening anxiety, it will be recorded and excluded. Patients who requested to participate in the music therapy sessions randomly assigned to the NMT group will receive the same MT as the MT group after completing the prescribed follow-up time (D14 and D28).

Patients in the MT group will receive individualised receptive MT supervised by a music therapist, along with required anti-cancer medications. Prior to starting MT, patients in the MT group will be introduced to the MT process for 5–10 min by the music therapist. The treatment room will be soundproofed, with patients in a resting or sitting position with eyes closed and relaxed. Prior to MT, patients in the MT group will be exposed to various types of music to determine their preferences. The repertoire for MT, which is nature-based sound, lasting 10–15 min, will be composed by the Department of Music Engineering of Shanghai Conservatory of Music. After recording each patient's music preferences during playback, no more than three music clips from each genre will be chosen for individualised music clips of total length about 20 min, increasing individual patient comfort and orientation and reducing anxiety. Subsequently, the music therapist will play the personalised music clip created for 20 min, at 15:00–16:00, once a day for 1 week. Studies have shown that intervention 1–3 days with MT 30–60 min per day is effective for depression and anxiety of various patients with cancer.[32–34] Simultaneously, another music therapist will use a psychoeducational approach in conjunction with verbal instructions. The psychoeducational approach in conjunction with verbal instruction includes: (1) informing the patient of the purpose and duration of the treatment; (2) adjusting the appropriate volume; (3) instructing the patient how to adjust breathing and relax methodically from head to feet to the rhythm of the music. Conditions for music therapy will include: (1) no bright light interference; (2) the patient in a resting or inactive state; and (3) music played through speakers at a volume controlled between 45% and 65%.

All participants will be required to complete STAI, Distress Thermometer (DT), HAMA and Quality of Life Questionnaire C30 (QLQ-C30) instruments on the day before and the day after treatment, as well as 14 and 28 days after treatment. The total scores of these items will be calculated and their differences in the MT and NMT groups will be compared. Blood samples will be collected for ELISA analysis of cytokine levels (serum IL-1β, TNF-α, IL-2R, IL-4, IL-6, IL-8 and IL-10) and neurotransmitter levels (5-HT, dopamine, norepinephrine, adrenocorticotropic hormone and γ-aminobutyric acid). Gut microbiota will be collected on the day after treatment, then be analysed by 16sRNA. Changes in primary disease condition will also be recorded. Music intervention flow is shown in table 1.

Data collection

Members of the Department of Oncology, Yueyang Hospital of Integrated Traditional Chinese and Western Medicine, Shanghai University of Traditional Chinese Medicine will collect and evaluate data from inpatients at screening and baseline, as well as during and after intervention and at follow-up periods.

Enrolment and baseline

Patients will be screened at admission using inclusion and exclusion criteria. Information collected from patients who qualified will include important demographic characteristics, such as age, sex, education and marital status, and general clinical characteristics, including type of disease, disease stage, surgical history, current treatment and previous treatment. All included patients will complete the STAI, DT, HAMA and QLQ-C30. The STAI consists of 40 items, each of which is graded on a 4-point scale with S-AI levels of 1 for not at all, 2 for somewhat, 3 for moderately and 4 for very significantly; and T-AI levels of 1 for almost never, 2 for occasionally, 3 for frequently and 4 for almost always; with 10 reverse scores. Reverse scoring will be given in order 4, 3, 2 and 1 to calculate cumulative scores for the S-AI and T-AI scales, with a minimum score of 20 and a maximum score of 80. The total S-AI score will reflect the severity of each subject's current anxiety symptoms, whereas the total T-AI score will reflect each subject's consistent or usual anxiety, with higher scores indicating more severe anxiety,[35 36] and no specific cut-offs exist.[6] Referring to previous studies, we defined 'high anxiety' as a score of STAI ≥40.[37] The DT uses distress scores to determine each patient's level of psychological distress which includes a Visual Analogue Scale score and a problem list.[38–40] The HAMA consists of 14 items, with symptoms graded on a 5-point scale from

Table 1 Music intervention

Groups	Intervention	Time point	Scales	Indicators
NMT groups	Emotional nursing care: symptoms inquiry, timely communication when emotional distress occurs	Inquiry and communication: 20 min, at 15:00–16:00, once a day for 1 week	STAI DT HAMA QLQ-C30	Blood test: cytokines and neurotransmitters; gut microbiota
MT groups	Emotional nursing care and individualised receptive MT: 1. Music clips: according to patient's music preferences 2. MT includes the psychoeducational approach: (1) informing the patient of the purpose and duration of the treatment; (2) adjusting the appropriate volume; (3) instructing the patient how to adjust breathing and relax methodically (head–face–neck–shoulders–arms, hands–chest–abdomen–low back–buttocks–legs–calves–feet) to the rhythm of the music	MT: 20 min, at 15:00–16:00, once a day for 1 week Inquiry and communication: before MT	STAI DT HAMA QLQ-C30	Blood test: cytokines and neurotransmitters; gut microbiota

DT, Distress Thermometer; HAMA, Hamilton Anxiety Scale; MT, music therapy; NMT, non-music therapy; QLQ-C30, Quality of Life Questionnaire C30; STAI, State-Trait Anxiety Inventory.

Table 2 Clinical trial procedure

	Trial period				
	Allocation	Intervention start	Intervention finish	Follow-up	
Day	D0	D1	D7	D14	D28
Enrolment					
Informed consent	√				
Inclusion	√				
Exclusion	√				
Basic information	√				
History	√				
Efficacy indicators					
STAI		√	√	√	√
DT		√	√	√	√
HAMA		√	√	√	√
QLQ-C30		√	√	√	√
IL-1β, TNF-α, IL-2R, IL-4, IL-6, IL-8 and IL-10		√	√		
5-HT, DA, NE, ACTH and GABA		√	√		
Gut microbiota		√	√		
Safety indicators					
Vital signs	√		√		
Blood, liver and kidney functions	√		√		
Adverse events			√	√	√
Other parameters					
Adherence evaluation			√		
Analysis of shedding causes			√		
Efficacy evaluation			√		

ACTH, adrenocorticotropic hormone; DA, dopamine; DT, Distress Thermometer; GABA, γ-aminobutyric acid; HAMA, Hamilton Anxiety Scale; 5-HT, 5-hydroxytryptamine; IL, interleukin; NE, norepinephrine; QLQ-C30, Quality of Life Questionnaire C30; STAI, State-Trait Anxiety Inventory; TNF-α, tumour necrosis factor-α.

0 to 4, with 0 indicating no symptoms; 1 indicating mild symptoms; 2 indicating moderate symptoms; 3 indicating severe symptoms; and 4 indicating extremely severe symptoms. The cut-off value for HAMA was a total score of 14. Total scores ≥29, ≥21, ≥14, ≥7 and <7 were indicative of severe anxiety, significant pressure, anxiety, probable anxiety and no anxiety, respectively.[41] The QLQ-C30, which will be used to assess quality of life, has shown high

Table 3 Primary and secondary outcomes

Outcome measures	
Primary outcomes	
Assessment of the effects of MT on symptoms of anxiety in patients with cancer with anxiety	1. STAI will be used to detect transient anxiety and stable anxiety tendency in patients with cancer
	2. HAMA will be used to evaluate the severity of anxiety symptoms in patients with cancer
	3. DT will be used to determine the level of psychological distress in patients with cancer
Secondary outcomes	
Assessment of the effects of MT on quality of life and immune-related blood indices in patients with cancer with anxiety	1. QLQ-C30 will be used to assess the quality of life and overall health status of patients with cancer with anxiety
	2. Blood index and physiological indicators will be used to assess changes in serum concentrations of cytokines (IL-1β, TNF-α, IL-2R, IL-4, IL-6, IL-8 and IL-10) and neurotransmitters (5-HT, DA, NE, ACTH and GABA) in patients with cancer with anxiety before and after treatment
	3. Gut microbiota will be collected to compare the differences in diversity, enterobacteriaceae and short-chain fatty acids

ACTH, adrenocorticotropic hormone; DA, dopamine; DT, Distress Thermometer; GABA, γ-aminobutyric acid; HAMA, Hamilton Anxiety Scale; 5-HT, 5-hydroxytryptamine; IL, interleukin; NE, norepinephrine; QLQ-C30, Quality of Life Questionnaire C30; STAI, State-Trait Anxiety Inventory; TNF-α, tumour necrosis factor-α.

reliability and validity in patients with cancer. The QLQ-C30 was given as a self-assessment, with a total of 30 entries, including five functional subscales: somatic functioning, role functioning, cognitive functioning, emotional functioning and social functioning; three symptom subscales: fatigue, pain, and nausea and vomiting; and six single-symptom measures: dyspnoea, insomnia, loss of appetite, constipation, diarrhoea, economic hardship and an overall quality of life scale. A higher functional scale score indicates a better quality of life, whereas a higher symptom scale score indicates a worse quality of life.[42]

Adherence and follow-up

During the treatment period, patients will be hospitalised at Yueyang Hospital of Integrated Traditional Chinese and Western Medicine, Shanghai University of Traditional Chinese Medicine, to facilitate follow-up; patients unable to be followed up as inpatient will undergo telephone follow-up by a research assistant. Patient schedules are shown in table 2.

Outcome measures

The primary and secondary outcomes are shown in table 3.

Quality control

To ensure the accuracy of the experiments, research assistants will review study documents, informed consent forms, case report forms (CRFs) and data records on a regular basis.

Data management

The team leader and research assistant will review the CRFs and scales before handing them over to data management staff for data entry and administration. The original CRFs and all scales (including consent forms) will be kept at the Department of Oncology, Yueyang Hospital of Integrated Traditional Chinese and Western Medicine, Shanghai University of Traditional Chinese Medicine.

The Data and Safety Monitoring Board of the Clinical Assessment Center at Yueyang Hospital of Integrated Traditional Chinese and Western Medicine, Shanghai University of Traditional Chinese Medicine, which is made up of clinical experts and statisticians, will monitor the safety of the study every month.

Patient and public involvement

Patients and the general public will not be involved in the design of the study or in the determination of outcome measures. No attempt will be made to assess the burden of the intervention on the patients themselves.

Sample size

Based on previous studies, the level of STAI improvement will be regarded as the main indicator of efficacy, with differences of 5.43 regarded as the primary outcome, with a unilateral p=0.05. Sample size calculation will be done with PASS V.15.0 software using the formula:

$$n1 = n2 = \frac{\left| u_{a/2}\sqrt{2\bar{p}(1-\bar{p})} + u\beta\sqrt{p_1(1-p_1)+p_2(1-p_2)} \right|}{(p_1-p_2)2}$$

The minimum total sample size was calculated to be 48 patients. Including a 20% withdrawal rate, the minimum total sample size was 60 patients, or 30 in each group based on 1:1 randomisation.

Statistical analysis

Normally distributed continuous variables will be compared by t-tests and non-normally distributed continuous variables by Mann-Whitney rank-sum tests. Categorical variables will be compared by X^2 tests. SPSS V.22.0 will be used to generate a normal probability graph and perform a hypothesis test to check whether the observed values obeyed a normal distribution. Individual data points will be superimposed on a box-line plot for calculations. The results of anxiety correlation scales and ELISA will be compared by t-tests or Mann-Whitney rank-sum tests according to whether the normal distribution

is met or not. The results of 16sRNA will be classified by the RDP reference database (http://www.mothur.org/wiki/RDP_reference_files) to calculate the relative abundance of microbial communities at different levels. Then, the differences between samples (groups) will be calculated by Principal Component Analysis, Principal Coordinates Analysis, Non-Metric Multi-Dimensional Scaling, Unweighted Pair-group Method with Arithmetic Means and Beta Diversity Index Inter-group Difference Analysis. All statistical analyses will be performed by SPSS V.22.0 software, with $p < 0.05$ considered statistically significant. Patients who used other drugs or therapies on cancer will be stratified in statistical analysis.

Ethical issues

The study will adhere to the Helsinki Declaration and the Ethical Guidelines for Clinical Research. The study protocol has been approved by the Research Ethical Committee of Yueyang Hospital of Integrated Traditional Chinese and Western Medicine, Shanghai University of Traditional Chinese Medicine (approval number: 2019-092).

DISCUSSION

Anxiety and depression are associated with cancer mortality and survival rates.[43] The increased focus on quality of life of patients with cancer has increased interest in their emotional symptoms. MT may reduce anxiety and depression, and improve the quality of life of patients with cancer.[44–46] MT is a risk-free, flexible operation and cost-effective intervention that may improve anxiety in patients with cancer. The RCT described in this study will test whether this non-pharmacological intervention can reduce anxiety in patients with cancer. Findings of this study may serve as a reference for trials determining whether other non-pharmacological methods could improve anxiety symptoms in oncology patients.

A major strength of the present trial is its method of intervention, in which individual patients are exposed to a personalised music clip based on each patient's preference. Outcomes will be measured using the STAI, DT, HAMA and QLQ-C30 instruments. HAMA scores are measured by physicians, making them more objective. STAI can respond to both short-term and long-term emotional traits. The STAI and HAMA scales will therefore be combined to reduce bias and increase the reliability of the results. Moreover, this study will measure the levels of neurotransmitters, gut microbiota and cytokines in patients with tumour to explore the mechanisms by which MT improves anxiety in patients with tumour. A meta-analysis reported that high levels of IL-8 and IL-6 were significantly associated with the prognosis of patients with cancer treated with immune checkpoint inhibitors.[47] Moreover, serum IL-6 levels can be used as a biomarker to predict the outcome of treatment with antidepressants.[48] A case–control study found that faecal microbiota signatures differed in patients with gastrointestinal cancer with and without anxiety and depression.[49] The gut–brain–microbiota axis could modulate depression and anxiety induced

by chronic stress through ileal immune regulation.[50] In addition, MT could increase salivary immunoglobulin A levels and reduce cortisol levels of patients with cancer.[51] MT can significantly increase natural killer cell count and activity.[52] Therefore, we will assess the effects of MT on the efficacy of immunotherapy in patients with cancer in the future studies.

This study, however, is still subject to some limitations. The major limitation is the single-centre nature of this trial, which may limit the generalisability of study results. In addition, the intervention period will be only 1 week, which may be too short to determine the effects of MT on immune function and gut microbiota. Future studies should be designed to test whether longer periods of MT are of greater benefit in patients with cancer.

Trial status

The first participant will be enrolled in December 2022 and the study is expected to end in December 2023.

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