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Liuzijue is a promising exercise option for rehabilitating discharged COVID-19 patients

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Abstract

Background: Among discharged COVID-19 patients, the health-related quality of life is poor, and patients suffer from significant physical and psychological impairment. This study was designed to investigate the effects of Liuzijue exercise on the rehabilitation of COVID-19 patients.

Methods: Thirty three eligible patients with COVID-19 were enrolled in the study after discharge. All the participants practiced Liuzijue exercise once per day for 20 minutes over 4 weeks. Data were collected at baseline and the end of the intervention. Primary outcomes involved functional capacity and secondary outcomes involved quality of life.

Results: The maximal inspiratory pressure (MIP), peak inspiratory flow (PIF), and diaphragm movement in deep breathing (DM-DB) of patients increased significantly after 4 weeks of intervention. The dyspnea was also alleviated and exercise capacity was significantly improved. In terms of quality of life, physical functioning and role-physical scores were significantly increased. Moreover, Liuzijue could significantly alleviate the depression and anxiety status of the patients.

Conclusion: Liuzijue exercise is a viable alternative home exercise program that produced better functional capacity and quality of life in discharged patients with COVID-19. These findings also showed the necessity of rehabilitation intervention for cured COVID-19 patients.

Abbreviations: 6WMT = 6-Minute Walk Test, BP = bodily pain, COPD = chronic obstructive pulmonary disease, DM = diaphragm movement, DT = diaphragm thickness, GH = general health, HAMA = Hamilton Anxiety Rating Scale, HAMD = Hamilton Depression Scale Rating Scale, MH = mental health, MIP = maximal inspiratory pressure, mMRC = modified British Medical Research Council, PF = physical functioning, PIF = peak inspiratory flow, RE = role-emotional, RP = role-physical, SF = social functioning, SF36 = Short Form 36 Item Health Survey, TCEs = traditional Chinese exercises, VT = vitality.

Keywords: coronavirus disease-2019, exercise, Liuzijue, rehabilitation, respiratory function

1. Introduction

The ongoing COVID-19 pandemic, the disease caused by the SARS-CoV-2 coronavirus, has created challenges for governments around the world to balance public safety and economy. The COVID-19 mortality rate varies greatly across countries; it is around 3.7% in China according to its official national statistics.[1,2] However, there is currently no proven treatment for COVID-19 management to date. Globally, more than 18 million people have been infected and more than 690,000 have died from COIVD-19 as of August 4, 2020. A subset of patients rapidly develops severe pneumonia and complications including acute respiratory distress syndrome, pulmonary edema, acute kidney injury, or multiple organ failure.[3–5] As SARS-CoV-2 enters through the airways and mainly attacks the respiratory tract, recovered patients often have varying degrees of parenchymal lung damage.[6] Among discharged COVID-19 patients, the health-related quality of life is poor, and patients suffer from significant physical and psychological impairment.[7] Therefore, it is extremely urgent to perform safe and effective rehabilitation intervention for discharged COVID19 patients.

Traditional Chinese exercises (TCEs), such as Tai Chi, Liuzijue, and Yijinjing, are fitness methods that improve human health. In China, it is estimated that more than 100 million people practice TCEs. TCEs are regarded as a form of mind-body intervention for the treatment of various chronic diseases.[8]

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The data used to support the findings of this study are available from the corresponding author upon request.

The authors have no conflicts of interests to disclose.

The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

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Among the TCEs, Liuzijue, one of the New Health Exercise Series compiled by the China Qigong Management Center, is the most popular exercise in ancient Chinese literature.[9,10] Liuzijue involves inhalation and exhalation through different mouth patterns to regulate and control the rise and fall of the breath in the body. It is performed by producing 6 different sounds, ("xu", "hē", "hu", "sī", "chuī", and "xī") through expiration together with corresponding body movements. Recent studies suggest that Liuzijue can effectively improve pulmonary function, exercise capacity, and quality of life in patients with chronic obstructive pulmonary disease (COPD).[11,12] However, the effect of Liuzijue exercise in patients who have been infected with SARS-CoV-2 coronavirus remains unknown. An effective home-based rehabilitation program should be explored for patients who have recovered from COVID-19.

The current study aimed to address the necessity of rehabilitation intervention for cured COVID-19 patients, and to examine the effect of Liuzijue on the pulmonary function, quality of life, and mental status of discharged COVID-19 patients. We hypothesized that Liuzijue, as an alternative home exercise program, would demonstrate differential improvements in psychological and physiological disorder after 4 weeks of intervention.

2. Methods

2.1. Study design

This study was a multicenter prospective self-controlled study to explore the effects of Liuzijue in discharged COVID-19 patients (Fig. 1). Patients were screened using the inclusion and exclusion criteria listed in Table 1. Eligible patients were recruited from the First Affiliated Hospital of Nanchang University, First People's Hospital of Jiujiang, and Xinyu People's Hospital; all patients participated in this study voluntarily. The enrolled patients were instructed to practice a Liuzijue exercise routine once a day for 20 minutes over 4 weeks (Fig. 2). Data were measured before and after interventions. This clinical study was approved by the Clinical Research Ethics Committee of the First Affiliated Hospital of Nanchang University and written informed consent was obtained from each subject. This study was registered with the Chinese Clinical Trial Registry (ChiCTR2000030933).

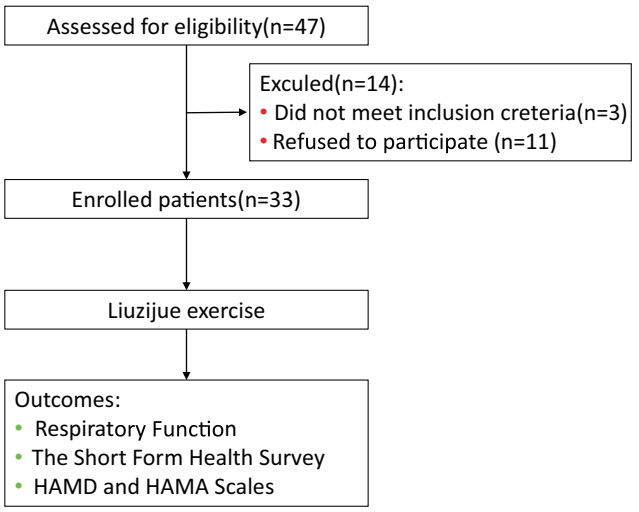

Figure 1. Flow chart of this pilot study.

Table 1

Inclusion and exclusion criteria of this clinical trial.

Inclusion criteria	Exclusion criteria
Patients diagnosed with COVID-19, and meets the discharge criterion*	Patients with severe primary disease of liver, kidney, hematological and endocrine system
Older than 18 years old	Patients with unstable vital signs
Be conscious	Patients with a history of psychosis, substance abuse or dependence
Volunteer to participate in the study and sign the informed consent form	Pregnant or lactating women

*In accordance with the diagnostic criteria of the Diagnosis and Treatment Plan of the Novel Coronavirus Pneumonia (7th Version of Trial Implementation) issued by the National Health Commission of the People's Republic of China.

2.2. Respiratory muscle function

Maximal inspiratory pressure (MIP, cmH2O) and peak inspiratory flow (PIF, L/s) were measured by a respiratory therapist at the corresponding Hospital following a standardized protocol using the POWERbreathe inspiratory muscle assessment system (POWERbreathe International Ltd., UK).

2.3. Measurement of diaphragm thickness (DT) and diaphragm movement (DM)

Ultrasonography was performed by an experienced operator using Aplio XG ultrasonography (Toshiba, Tokyo, Japan). The thickness of the diaphragm was assessed using B-mode ultrasound with a 7-MHz sector array transducer, and was visualized at the zone of apposition perpendicular to the chest wall between the 7th and 9th intercostal space in the anterior axillary lines inferiorly to the costophrenic angle. The right hemidiaphragm was measured at the end of inspiration.[13]

The right hemidiaphragm motion was examined using M-mode ultrasonography with a 3.5-MHz curved array transducer through the longitudinal semicoronal plane from a subcostal or low intercostal approach. The motion of the hemidiaphragm was captured during normal quiet breathing (DM-QB) and deep breathing (DM-DB) at the end of inspiration. All measurements were taken 3 times and the mean values were used for analysis.

2.4. Quality of life assessments

Health-related quality of life was evaluated using the Short Form 36 Item Health Survey (SF36),[14] a widely used generic questionnaire to assess patients' self-reported health status across 8 domains: physical functioning (PF), role-physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role-emotional (RE), and mental health (MH). The SF-36 questionnaire scores were transformed using a 0 (the worst possible score) to 100 (the best possible score) scale.

2.5. Psychological assessments

To assess the severity of anxiety-related and depressive symptoms, the Hamilton Depression Scale Rating Scale (HAMD) and the Hamilton Anxiety Rating Scale (HAMA) were used. The 17-item HAMD was applied to comprehensively assess the severity of depressive symptoms.[15] The 14-item HAMA was employed to comprehensively assess the severity of anxiety symptoms.[16]

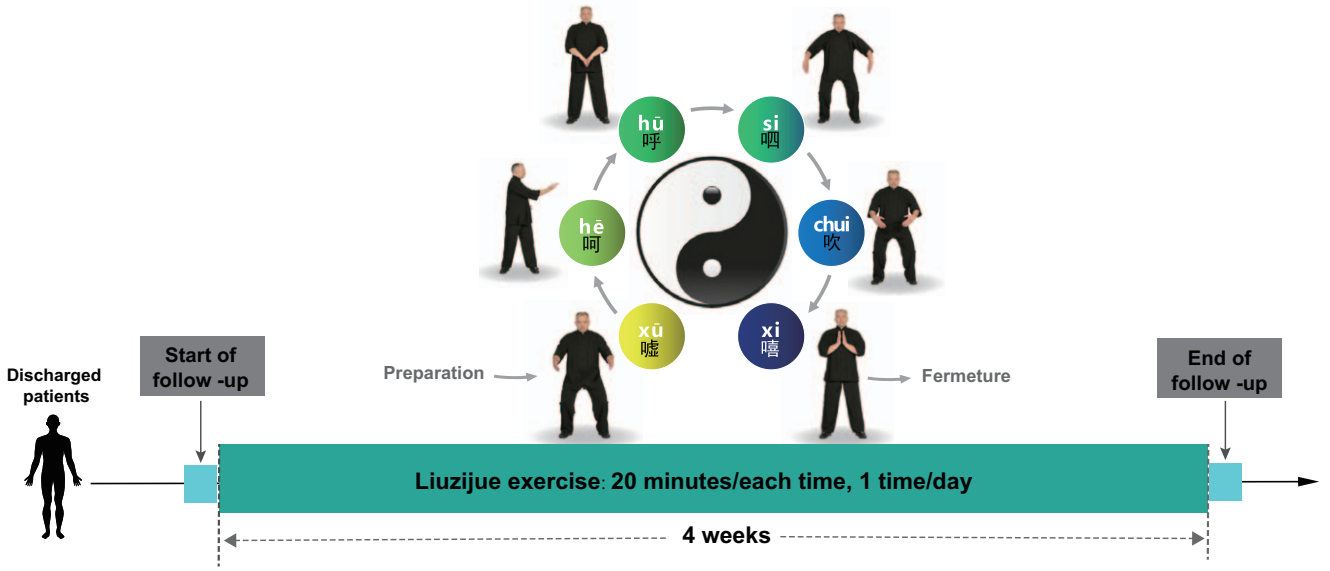

Figure 2. Experimental flow of the rehabilitation intervention.

2.6. Exercise capacity

To assess submaximal exercise capacity, the 6-Minute Walk Test (6MWT) was used.[17] The test measures how far an individual can quickly walk along a flat, hard surface in 6 minutes. As most activities of daily living are performed at submaximal levels of exertion, the 6MWT test is a valid and reliable test of physical walking ability that has been related to aerobic fitness.

2.7. Dyspnea assessments

Dyspnea in patients was measured by using the modified British Medical Research Council (mMRC) scale.[18] The mMRC dyspnea scale is a simple 5-point scale corresponding to activities that provoke dyspnea, with scores ranging from 0 (short of breath only with heavy exertion) to 4 (shortness of breath with dressing or minor activities).

2.8. Statistical analysis

Continuous data (normal distribution) are presented as means ± standard deviation. Significant differences in these data before and after treatment were determined using a paired *t* test. For the non-normal distribution data, significant differences before and after treatment were assessed using the paired Wilcoxon test. Statistical analyses were conducted using GraphPad Prism 8.0 software. A P value $< .05$ was considered statistically significant.

3. Results

3.1. Characteristics of the subjects

Among the 47 discharged COVID-19 patients who enrolled in this study,3 patients did not meet the inclusion criteria and 11 patients refused to participate. Finally, 33 eligible patients were enrolled in this prospective self-controlled study (Fig. 1). The characteristics of the patients enrolled in the study are shown in Table 2. According to the clinical classification for COVID-19, there were 28 mild/moderate cases and 5 severe/critical cases were included. The means of age, height, weight, respiratory rate, heart rate, SBP, and DBP were 43.2 ± 10.4 (years), 165.3 ± 6.8 (cm), 67.6 ± 11.3 (kg), 21.3 ± 10.0 (breaths/minute), 78.0 ± 10.4 (beats/minute), 118.9 ± 20.2 (mm Hg), 118.9 ± 20.2 (mm Hg), respectively.

3.2. Respiratory function and exercise capacity

After 4 weeks of intervention, the MIP and PIF improved significantly. The mean increase in MIF was 13.46 ± 20.06

Table 2

Characteristics of the patients enrolled in the study.

Characteristics	Mild/Moderate (n = 28)	Severe/Critical (n = 5)	Total (n = 33)
Age (years)	42.9 ± 10.5	44.8 ± 11.0	43.2 ± 10.4
Sex			
Male	14 (50%)	3 (60%)	17 (51.6%)
Female	14 (50%)	2 (40%)	16 (48.5%)
Height (cm)	164.0 ± 6.3	170.6 ± 6.9	165.3 ± 6.8
Weight (kg)	65.3 ± 10.2	77.8 ± 10.9	67.6 ± 11.3
Respiratory Rate (times/min)	21.9 ± 11.1	18.6 ± 1.7	21.3 ± 10.0
SBP (mm Hg)	118.5 ± 20.3	121.1 ± 22.1	118.9 ± 20.2
DBP (mm Hg)	76.4 ± 15.7	71.4 ± 12.9	75.4 ± 15.2
Heart Rate (beat/min)	78.5 ± 11.2	75.8 ± 6.2	78.0 ± 10.4

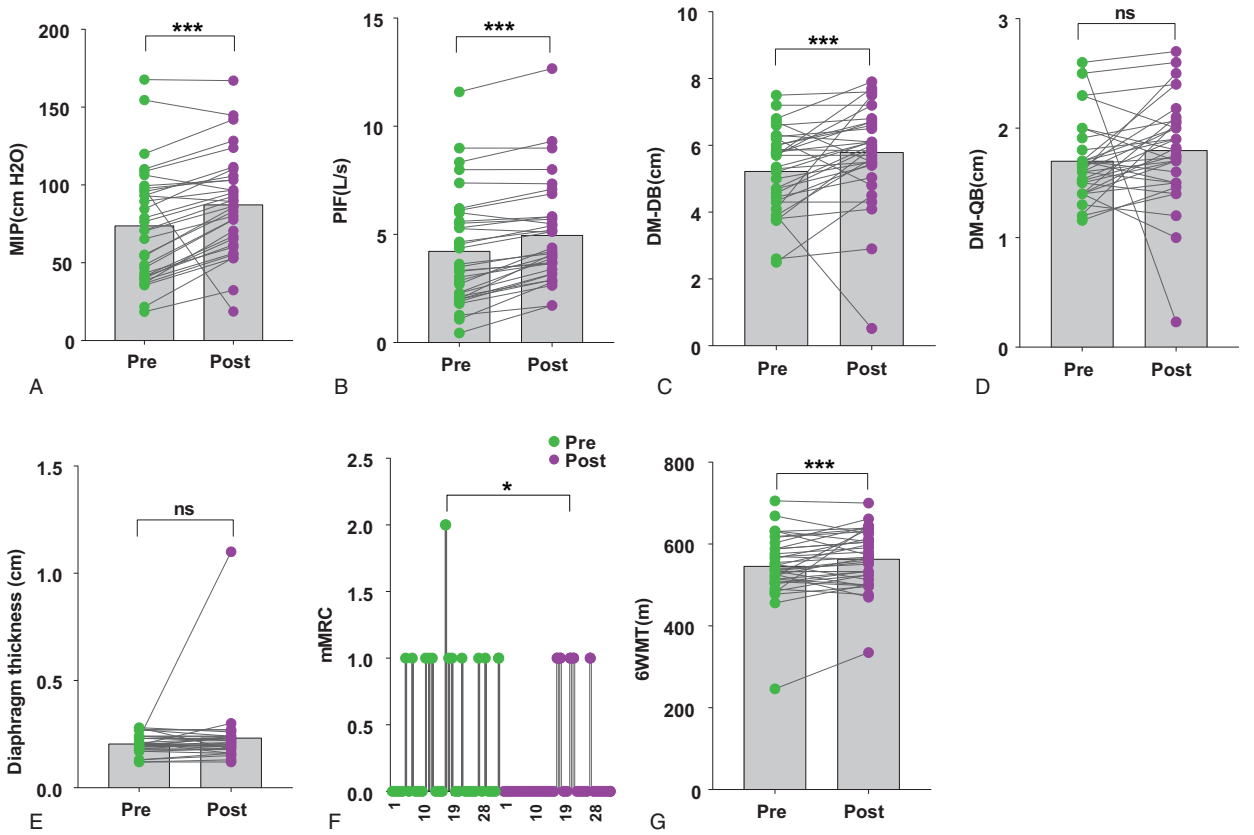

Figure 3. Respiratory muscle function and exercise capacity after 4 weeks of rehabilitation intervention. (A) Maximan inspiratory pressure (MIP), (B) peak inspiratory flow (PIF), (C) diaphragm movement (DM) in deep breathing (DB), (D) DM in quiet breathing (QB), (E) Diaphragm thickness (DT), (F) modified Britich Medical Research Council dyspnea scale (mMRC), (G) 6-Minute walk test (6WMT). ns = no significant; Pre = pretreatment, Post = posttreatment; $^{*}P < .05$; $^{***}P < .001$.

cmH2O ($P < .001$, Fig. 3A), and in PIF, 0.74 ± 0.58 L/second ($P < .001$, Fig. 3B). It was also found that DM-DB was increased, with a mean of 0.57 ± 1.18 ($P = .009$, Fig. 3C). However, there was no difference in DT DM-QB (Fig. 3D and E). Moreover, by using the mMRC scale, we found that Liuzijue could relieve dyspnea in patients ($P = .022$).

To further assess the effect of Liuzijue exercise on the exercise capacity, we performed 6WMT tests. Post the intervention, the 6-minute walk distance increased by 17.22 ± 43.78 m ($P = .020$, Fig. 3G).

3.3. Patients' quality of life

SF36-PF and SF36-RP scores increased significantly when compared to the baseline levels (SF36-PF: $P = .014$, Fig. 4A; SF36-RF: $P = .009$, Fig. 4B). For the rest of scale scores, including BP, GH, VT, SF, RE, and MH, these scores did not significantly change ($P > .05$, Fig. 4C–H).

3.4. Mental status

The HAMD and HAMA were applied to evaluate the patients' depression and anxiety status, respectively. The HAMD and HAMA scores were reduced significantly at the end of the follow-up period compared with the scores at the baseline (HAMD: $P = .0032$, Fig. 5A; HAMA: $P < .001$, Fig. 5B).

4. Discussion

In the present study, we applied the MIP, PIF, DT, and DM to reflect the respiratory muscle strength and function. After 4 weeks of the intervention, the MIP, PIF, and DM-DB improved significantly. By using the mMRC scale, it was found that Liuzijue reduced unpleasant symptoms of breathlessness. The 6WMT results also showed the exercise capacity was improved at the end of follow-up. These results indicated that Liuzijue may be a promising exercise option for the rehabilitation of patients who have had COVID-19. In terms of the quality of life, only the SF36-PF and SF36-RP scores were significantly increased. There was no significant difference between the pre- and postintervetion scores in SF36-BP, SF36-GH, SF36-VT, SF36-SF, SF36-RE, and SF36-MH. Therefore, Liuzijue may not result in the improvement of all aspects of quality life, but there has some benefit in the recovery of physical functions and role-physical. As for the impact of Liuzijue on mental status, the HAMA and HAMD scores significantly decreased; Liuzijue could alleviate the symptoms of depression and anxiety in patients.

COVID-19 was first reported by local health facilities in Wuhan, the capital of Hubei, China, in late December 2019.[19] It has since become a pandemic. However, the origins of the novel coronavirus are still unknown. To date, no effective treatments exist for COVID-19 management. Clinical practitioners and researchers are working to find effective treatments for COVID-

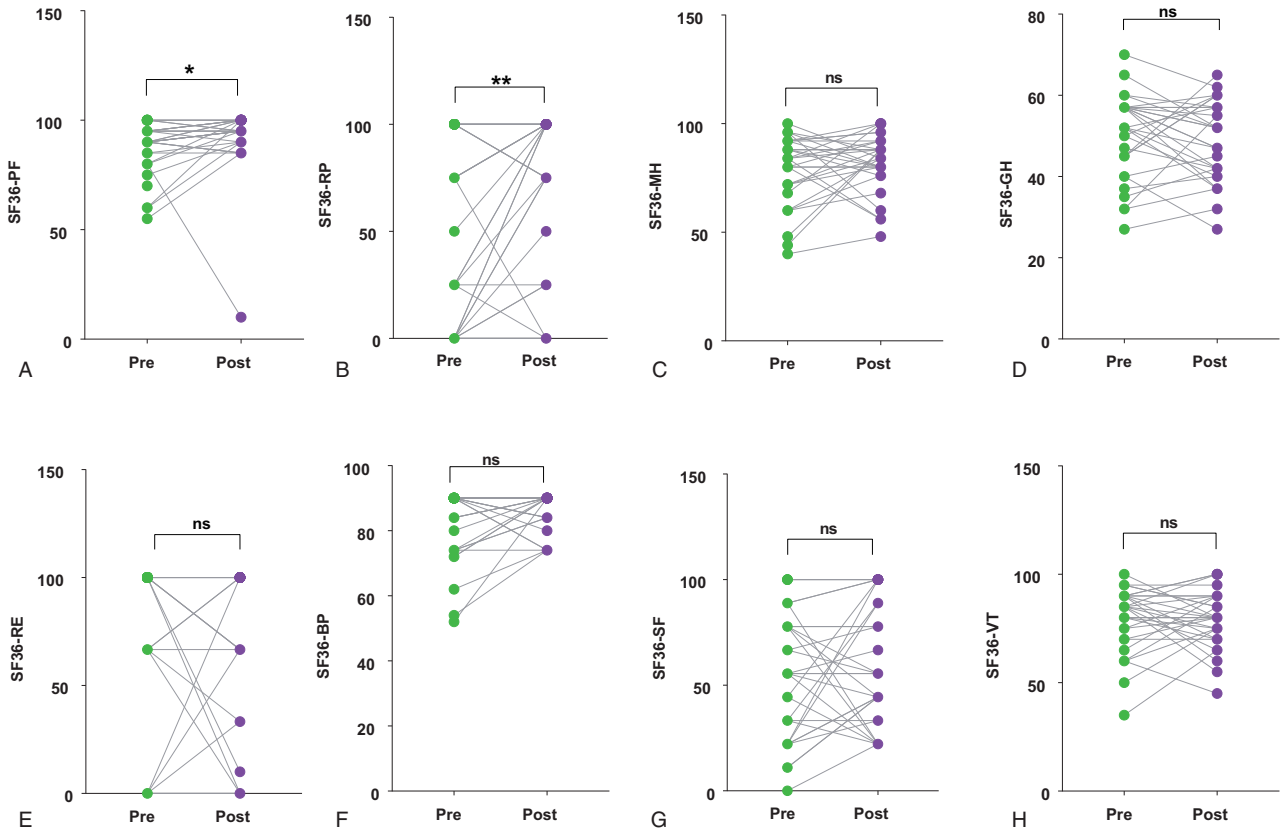

Figure 4. Change in the quality of life based on the Short Form 36 Item Health Survey (SF36). (A)SF36-physical functioning (PF), (B) SF36- role-physical (RP), (C) SF36-mental health (MH), (D) SF36- general health (GH), (E) SF36- role-emotional (RE), (F) SF36-bodily pain (BP), (G) SF36- social functioning (SF), (H) SF36- vitality (VT). ns = no significant, Pre = pretreatment, Post = posttreatment; $^{*}P < .05$; $^{***}P < .001$.

19, and complementary and alternative medicine may be a feasible and valuable option. To the best of our knowledge, this is the first clinical study to evaluate the potential efficacy of Liuzijue exercises in the rehabilitation of discharged COVID-19 patients.

Exercise training, an important part of pulmonary rehabilitation, has been shown to improve dyspnea and the health status of patients, and decrease healthcare use.[20–22] Exercise training should be one of the vital approaches in the rehabilitation of COVID-19 patients. In China, TCEs have played important roles in the battle against COVID-19. During the outbreak, in isolated mild cases in the Fangcang Hospitals and field hospitals of Wuhan Baduajin exercise, a part of traditional Chinese medicine, was practiced. These traditional Chinese exercises had already been widely used in the prevention and treatment of respiratory

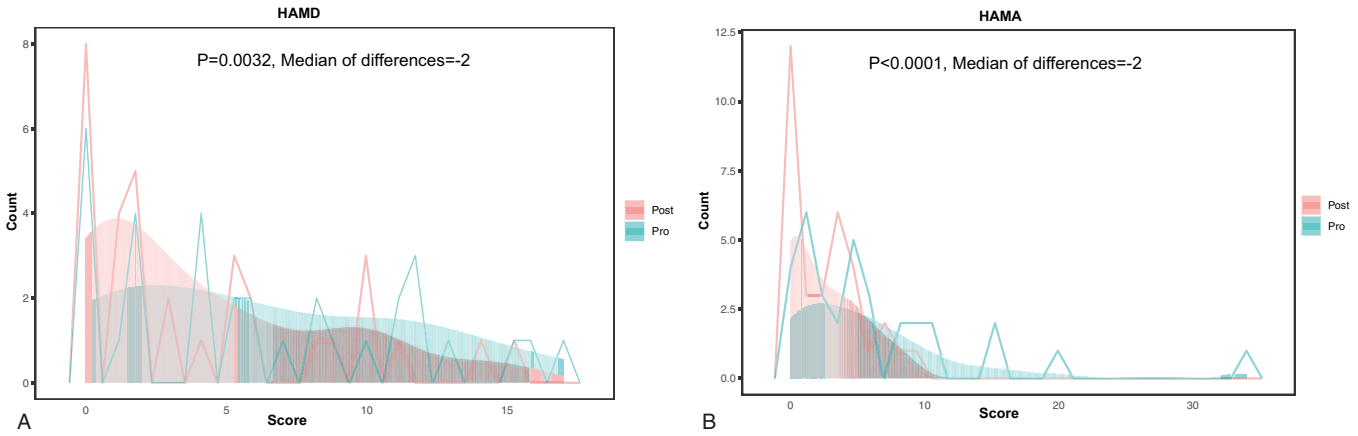

Figure 5. The scores of psychological assessments. (A) Hamilton Depression Scale Rating (HAMD), (B) Hamilton Anxiety Rating Scale (HAMA). Pre = pretreatment, Post = posttreatment.

infections because the movements in these exercises are smooth with low intensity and easy to learn. Liuzijue combines abdominal breathing and pursed lip breathing with uttering 6 different sounds, along with corresponding mild-body movements and a calm state of mind.

Among the discharged COVID-19 patients, the health-related quality of life was poor, and patients suffered from significant physical and psychological impairment.[7] Therefore, it is urgent to perform safe and effective rehabilitation interventions for discharged COVID19 patients. The present study demonstrated that Liuzijue exercises improved the respiratory function and exercise capacity of patients previously infected with the SARS-CoV-2 coronavirus at 4-weeks follow-up. In addition, the results in this study also showed Liuzijue exercises may improve the patients' quality of life and mental states. These results indicate that rehabilitation training is crucial for COVID-19 patients.

However, there are several limitations in this study. First, this is a multicenter, prospective, self-controlled study. Future well-designed randomized controlled trial studies will enhance the understanding of the effects of Liuzijue. Second, the sample size of this study was limited, which is explained by the control of the COVID-19 epidemic in the short period in Jiangxi province. We were unable to get larger samples.

Our results show that Liuzijue exercise can be an alternative home exercise program that produces better functional capacity and quality of life in discharged COVID-19 patients. These findings also showed the necessity of rehabilitation for discharged COVID-19 patients.

Author contributions

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Writing – original draft: Zhen Feng.
Writing – review & editing: Zhen Feng.

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