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Original Article

Effect of qigong exercise and acupressure rehabilitation program on pulmonary function and respiratory symptoms in patients hospitalized with severe COVID-19: A randomized controlled trial

Shu-ting Liu [a,1], Chao Zhan [b,1], Yun-jing Ma [c], Chao-yang Guo [a], Wei Chen [b], Xiao-ming Fang [b], Lei Fang [a,*]

[a] Shanghai University of Traditional Chinese Medicine, Shanghai, China
[b] Huangshi Hospital of Traditional Chinese Medicine, Hubei, China
[c] Department of Rehabilitation, Shanghai East Hospital, Shanghai, China.

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ABSTRACT

Background: There are several effective complementary and integrative therapies for patients with severe COVID-19. The trial aims to evaluate the efficacy and advantages of the qigong exercise and acupressure rehabilitation program (QARP) for treating patients with severe COVID-19.

Methods: A total of 128 patients with COVID-19 aged 20 to 80 years were recruited and randomly allocated in a 1:1 ratio to receive QARP plus standard therapies or standard therapies alone. QARP consisted of acupressure therapy and qigong exercise (*Liu Zi Jue*). The primary outcome was measured with the modified Medical Research Council (mMRC) dyspnea scale, and the secondary outcomes included the modified Borg dyspnea scale (MBS), fatigue Scale-14 (FS-14), patient health questionnaire-9 scale (PHQ-9), duration of respiratory symptoms, and vital signs.

Results: In total, 128 patients completed the clinical trial. The QARP group and standard therapies group showed significant improvements in vital signs (except blood pressure) and clinical scales compared with baseline ($p<0.05$). The QARP group also showed more significant improvement in the mMRC dyspnea scale (-1.8 [-2.1, -1.6], $p=0.018$) and modified Borg dyspnea scale (-3.7 [95% confidence intervals (CI) -4.3, -3.1], $p=0.045$). The duration of cough was 14.3 days (95% CI 12.6, 16.1, $p=0.046$), and the length of hospital stay was 18.5 days (95% CI 17.0, 20.0, $p=0.042$) in the QARP group, both of which were significantly reduced compared with the standard therapies group ($p<0.05$).

Conclusion: QARP plus standard therapies improved lung function and symptoms such as dyspnea and cough in patients with severe COVID-19 and shortened the length of hospital stay. Therefore, QARP may be considered an effective treatment option for patients with severe COVID-19.

Trial registration: Clinical Research Information Service Identifier: ChiCTR2000029994

1. Introduction

Since the beginning of the coronavirus disease 2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), 119,220,681 confirmed cases, including 2,642,826 deaths, have been reported by the World Health Organization as of March 14, 2021.[1] Most severe cases present with dyspnea, pneumonia, and respiratory failure.[2,3] Therefore, the treatment of respiratory symptoms and lung function is particularly critical. Evidence[4-5] shows that acupuncture can effectively improve lung function, dyspnea, and quality of life with pneumonia. Moreover, qigong exercise can improve respiratory function and enhance exercise levels. Qigong exercise has therapeutic effects and affects the stable phase of the later stage of COVID-19[6–8] and is compatible with a telerehabilitation approach that minimizes contact with COVID-19 patients to prevent transmission of infection. Therefore, the aim of this trial was to determine the efficacy of qigong exercise and acupressure rehabilitation program (QARP) for treating patients with severe COVID-19.

* Corresponding author at: Shanghai University of Traditional Chinese Medicine, Shanghai 201203, China.
E-mail address: fanglei586@126.com (L. Fang).
[1] These authors contributed equally to this work.

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2. Methods

2.1. Trial registration

The study was registered with the China Clinical Trial Registry (ChiCTR2000029994; https://www.chictr.org.cn/showproj.aspx?proj=49309).

2.2. Ethical statement

The Ethics Committee of Huangshi Hospital of Traditional Chinese Medicine approved the trial protocol (item number: HSZYYJ-2020-003-01). In addition, all patients signed informed consent before being enrolled in the study.

2.3. Study design

The study design was a single-center, parallel-arm, randomized controlled trial. Participants aged 20–80 years diagnosed with COVID-19 according to National Diagnostic and conforming to the treatment protocol (the latest trial version) were recruited from among inpatients at Huangshi Hospital of Traditional Chinese Medicine. The protocol was written and mediated in accordance with the CONSORT (Consolidated Standards of Reporting Trials) statement and published.[9]

2.4. Inclusion and exclusion criteria

Patients were included if they met each of the following conditions: (1) critical diagnostic criteria for severe COVID-19,[10] (2) aged between 20 and 80 years, (3) stable condition and conscious and cooperative during the examination, (4) willing to participate in the trial and sign the informed consent form, and (5) agreed to refrain from other exercise programs.

Patients who met any one of the following conditions were excluded from the trial: (1) complications due to other underlying severe diseases, such as chronic obstructive pulmonary disease, obstructive pulmonary disease, coronary heart disease, and hypertension, (2) serious mental illness, (3) cognitive dysfunction preventing an understanding of the trial process and rehabilitation content, (4) severe bone and joint diseases (such as spinal arthritis, severe osteoporosis, and periarthritis) affecting limb function and movement, (4) respiratory failure requiring mechanical ventilation or shock or combined organ failure requiring intensive care unit (ICU) monitoring and treatment, (5) pregnant or lactating, and (6) participation in other forms of exercise during the trial.

2.5. Dropout and suspension criteria

Participants had the right to withdraw from the research for any reason and without giving a reason.[11] Moreover, if the hospitalization time was less than seven days, the participants were excluded since the outcome evaluation could not be completed.

2.6. Randomization and masking

Between February 19 and March 31, 2020, 271 patients were screened for COVID-19. The number of patients screened accounted for 80% of the confirmed COVID-19 cases in Huangshi Hospital of Traditional Chinese Medicine during this period. Participants were randomly assigned to the Qigong Exercise and Acupressure Rehabilitation Program (QARP) group or standard therapies group. Randomization was performed following the eligibility and baseline assessment. The Department of Science and Technology of SHUTCM generated the randomization sequence using a random number generator (IBM, Chicago, IL, USA), and the sequence was subsequently placed in sequenced, sealed, opaque envelopes. When potential participants met the inclusion criteria, an envelope was opened, and the participant would accept the corresponding measures. Eligible patients were randomly divided into the standard therapies group and the QARP group with an allocation proportion of 1:1.

2.7. Interventions

2.7.1. Standard therapies group

Participants assigned to the standard therapies group received only standard guideline therapies drafted by the health authorities: (1) Adequate rest time for patients should be ensured, and close monitoring of vital signs, oxygen saturation, etc., by medical staff is necessary. (2) Additionally, routine blood and urine tests, C-reactive protein, biochemical indicators, blood coagulation function, arterial blood gas analysis, chest imaging, etc., should be monitored based on changes in condition. (3) Timely effective oxygen therapy measures should be taken; in particular, patients with severe disease should receive a nasal cannula or mask to inhale oxygen, and relief of respiratory distress and/or hypoxemia should be promptly evaluated. (4) Doctors should prescribe antiviral drugs combined with antibiotics if necessary. Drugs include antiviral therapy α-interferon (5 million U, twice a day, aerosol inhalation) + ribavirin (500 mg, 2-3 times a day, intravenous infusion), glucocorticoid treatment (methylprednisolone 0.5∼1 mg/kg/day), anticoagulant therapy (the recommended dose of subcutaneous injection of low molecular weight heparin was 100 UKg/q12h for 3-5 days) and tozumab (4∼8 mg/kg for the first dose, 400 mg for the recommended dose, cumulative number of doses up to 2 times, and the maximum dose for a single dose not exceeding 800 mg). (5) To maintain the stability of the internal environment, supportive treatment should be strengthened to ensure sufficient heat, and attention should be given to the water and electrolyte balance. (6) In addition, early Chinese medicine could be used to relieve symptoms.

2.7.2. The QARP group

The QARP group received QARP consisting of qigong exercise (Liu Zi Jue) and acupressure therapy, plus standard therapies. QARP was performed twice daily at 10 am and 4 pm. Therapists connected with patients via cameras for remote instruction exercises. The participants demonstrated qigong exercise live on the first day for the therapists, who had 10 years of relative clinical experience, until the participants were deemed competent. The participants were required to pronounce "Xu, He, Hu, Si, Chui, Xi" in a relaxed condition for 12 cycles. Guideline workbooks and videos of qigong exercise were used to facilitate subsequent practice. Each treatment lasted 20 min for a total of 40 min every day. The acupressure treatment was performed by a physical therapist every day after reaching a consensus on the participants' acupuncture points, pressure levels, and duration. The therapist pressed the acupoints with moderate force when the participants were in the sitting or supine position, with the pressure direction perpendicular to the skin surface for 3–7 s. The acupoints were Feishu (BL13), Danzhong (RN17), and Zhongfu (LU1), which are related to the lung viscera. The therapy was continued during the patient's stay until the day of discharge.

2.7.3. Outcomes

The outcomes were evaluated at two points (pretreatment and discharge) to reflect the changes in dyspnea and clinical symptoms of the patients with severe COVID-19. Patients were measured by remote assessment and questionnaire.

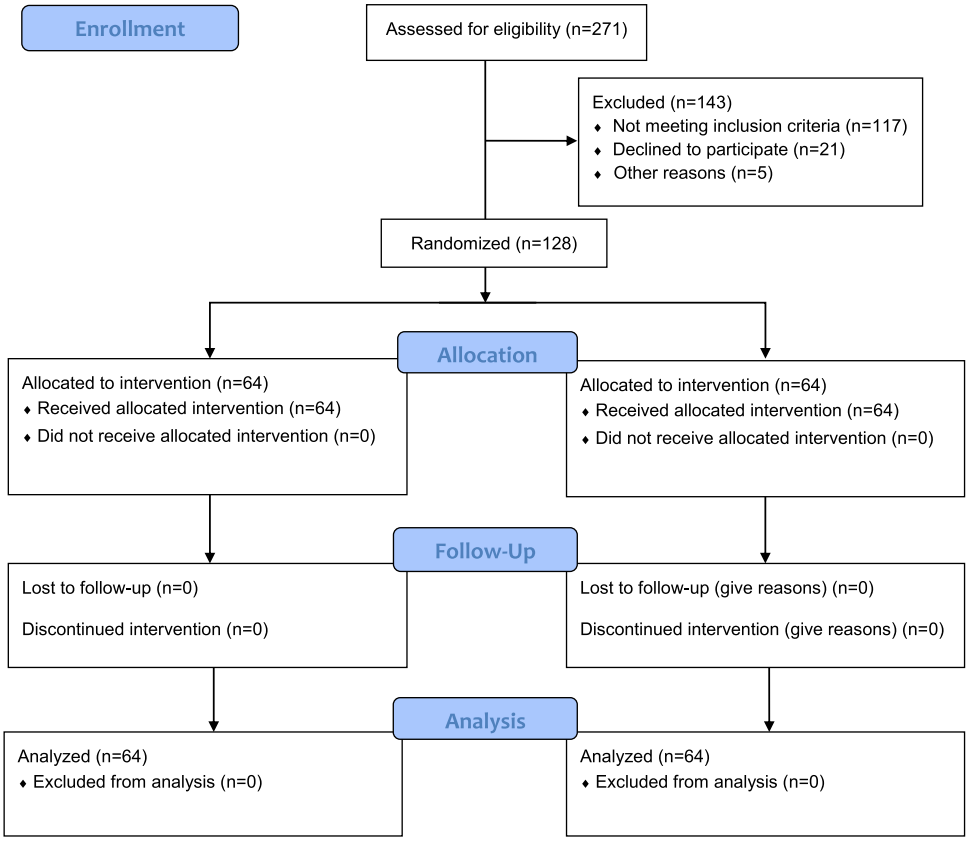

Fig. 1. CONSORT diagram of the eligibility, exclusion and randomization scheme. CONSORT, Consolidated Standards of Reporting Trials. QARP, Qigong Exercise and Acupressure Rehabilitation Program.

Table 1
Baseline demographic and clinical characteristics of patients at baseline.

Variable	QARP group (n=64)	Standard therapies group (n=64)	*p value*
Age	50.0 (47.2, 52.8)	53.6 (50.2, 57.0)	0.104
Sex			0.372
Men	25 (39.1%)	30 (46.9%)	-
Women	39 (60.9%)	34 (53.2%)	-
BMI (kg/m^2)	23.8 (23.1, 24.6)	23.9 (23.1, 24.7)	0.945
Any comorbidity			0.244
Hypertension	10 (16%)	10 (16%)	-
Diabetes	8 (13%)	5 (8%)	-
Chronic Hepatitis B	2 (3%)	1 (2%)	-
Chronic gastritis	2 (3%)	2 (3%)	-
Coronary heart disease	6 (9%)	1 (2%)	-
Chronic bronchitis	1 (2%)	0	-
Rheumatic heart disease	0	1 (2%)	-
Symptoms and signs			0.986
Cough	62 (97%)	61 (95%)	-
Fever	53 (83%)	52 (81%)	-
Dyspnea	48 (75%)	50 (78%)	-
Diarrhea	7 (11%)	9 (14%)	-
Fatigue	44 (69%)	47 (73%)	-
Temperature,°C	37.5 (37.3, 37.8)	37.4 (37.2, 37.6)	0.326
Heart rate (bpm)	85.5 (82.7, 88.4)	85.4 (82.3, 88.5)	0.941
Respiration rate (times/min)	23.1 (20.6, 25.6)	22.6 (21.6, 23.6)	0.728
Systolic blood pressure (mmHg)	124.2 (121.9, 126.6)	123.3 (119.9, 126.6)	0.648
Diastolic blood pressure (mmHg)	73.0 (70.7, 75.3)	72.5 (70.2, 74.9)	0.799
Blood oxygen saturation (SaO_2%)	92.7 (92.1, 93.2)	92.8 (92.1, 93.5)	0.778
MBS	5.5 (4.9, 6.1)	5.3 (4.8, 5.8)	0.663
FS-14	7.6 (6.8, 8.4)	7.2 (6.6, 7.9)	0.505
PHQ-9	13.3 (12.0, 14.7)	13.7 (12.3, 15.0)	0.717
mMRC	2.9 (2.7, 3.1)	2.7 (2.5, 2.8)	0.137

The data are presented as the mean (standard deviation [SD]) or median (interquartile range [IQR]) unless otherwise stated. QARP group intervention: qigong exercise and acupressure therapy + standard therapy for COVID-19; Standard therapies group intervention: standard therapy only.
BMI, body mass index; MBS, modified Borg dyspnea scale; FS-14, Fatigue Scale-14; PHQ-9, Patient Health Questionnaire-9 scale; mMRC, Medical Research Council; QARP, Qigong exercise and acupressure telerehabilitation program; SaO2, oxygen saturation; COVID-19, coronavirus disease of 2019.

2.7.3.1. Primary outcome. The primary outcome was measured with the modified Medical Research Council (mMRC) dyspnea scale, which has scores ranging from 0 to 4.[12,13] Higher mMRC values indicate a more severe degree of dyspnea.

2.7.3.2. Secondary outcomes. The secondary outcomes included the modified Borg dyspnea scale (MBS), fatigue Scale-14 (FS-14), patient health questionnaire-9 scale (PHQ-9), duration of respiratory symptoms, length of hospital stay and vital signs. The MBS assesses perceived exertion intensity.[14] The FS-14 consists of 14 entries, each of which is a fatigue-related question. The maximum total score is 14, and the higher the score, the more severe the fatigue. PHQ-9[15] detects and measures depression and its severity in medical populations in clinical settings. Respiratory symptoms include fatigue, cough, dyspnea, and some other nonspecific symptoms.

2.8. Sample size

The mMRC was used as the primary efficacy outcome. According to previous clinical studies of the effect of respiratory symptoms after acupressure therapy plus qigong exercise interventions, the mMRC scale score in the control group was 0.52 with a standard deviation of 0.11,[16], and the average mMRC Scale score in the treatment group was 0.95 with a standard deviation of 0.92. In this study, the target sample size was 64 participants in each group, anticipating a maximum loss to follow-up of 20%.

2.9. Statistical analysis

PASS software (PASS 11, NCSS, LLC, Kaysville, UT, USA) was used to estimate the sample size using two independent sample means (α=0.05, β=0.10). The primary endpoint was assessed in the intention-to-treat population of all randomized patients. The entire outcome scale was also measured at baseline. The data had a normal distribution; a two-way repeated-measure analysis of variance was used as the main analytic method, and a paired sample t-test was conducted between the two intervention groups. Categorical variables are presented as frequencies and percentages and were compared using the t-test. Significance was assigned at α <0.05 with a two-tailed test, and 95% confidence intervals are presented where appropriate. Statistical significance was set at $p < 0.05$. Statistical analysis was performed using IBM SPSS version 25.0 (IBM Corp., Armonk, NY, USA). A Kolmogorov–Smirnov test with Lilliefors correction was used to analyze all quantitative variables to determine whether they followed a normal distribution.

2.10. Patient and public involvement

Neither patients nor the public was involved in the design, conduct, reporting, or plans to disseminate this research.

3. Results

3.1. Study participants and baseline characteristics

Of 271 eligible patients, a total of 143 patients were excluded (117 patients did not meet the inclusion criteria, 21 declined participation, and 5 suffered adverse events). Finally, a total of 128 patients were recruited and completed this study (Fig. 1). Among the 128 patients, 64 patients each were randomly assigned to the QARP group or standard therapies group. The age, sex, and baseline demographics of each group were similar (Table 1). Cough, fever, dyspnea, and fatigue were the most common symptoms and signs. Diarrhea was infrequent.

3.2. Primary outcome

The primary efficacy analysis suggested that the improvement in mMRC from pretreatment to discharge was more positive in the QARP group than in the standard therapies group, and the QARP group had a more significant improvement of -1.8 in mMRC (p=0.018, Table 2).

3.3. Secondary outcomes

With the exception of blood pressure, all vital signs and clinical scales improved significantly in both the QARP group and the standard therapies group after treatment. There were significant differences in MBS (p=0.045, Table 2), cough symptoms (p=0.046, Table 3), and median hospital stay (p=0.042, Table 3) between the two groups. However, no significant differences in the PHQ-9 and FS-14 scales were observed between the two groups (Table 2).

4. Discussion

4.1. Summary of the main results

The results of this study showed that the integrated method of QARP plus standard therapies was more effective than the single standard therapies. After treatment, mMRC and MBS scores were significantly improved in both groups, and QARP was more effective in improving dyspnea. Given that the minimum clinically significant difference (MCID) is 0.5 for mMRC[17] and ≥1.0 for MBS,[18] our results indicate that QARP was very effective for improving the condition of patients with severe COVID-19. Furthermore, the durations of hospitalization and of cough were shorter in the QARP group than in the standard group. Accordingly, we believe that combining standard therapies with QARP has a greater clinical effect in patients with COVID-19 than standard therapies alone and may accelerate the patient recovery process.

4.2. Agreement and disagreement with other studies or reviews

Acupressure therapy and qigong exercise have been confirmed to have beneficial effects in patients with respiratory disease,[19-22] but few studies have applied them to patients with COVID-19. Two recent studies have suggested that qigong exercise may help improve respiratory symptoms and quality of life in patients with COVID-19. Tang et al.[23] studied the effects of qigong exercise on the rehabilitation of COVID-19 patients. However, that study did not combine qigong exercise with acupressure, and the participants were discharged patients with COVID-19. Zha et al.[24] studied the efficacy of modified rehabilitation exercises (MRE) for mild cases of COVID-19. In that study, MRE included acupressure on lung-associated acupoints but was derived from qigong exercise (eight-section Brocade). Therefore, it is not possible to directly compare the results of the present study with those of previous studies.

4.3. Potential mechanism of action

The pathophysiology of COVID-19 involves the secretion of a large amount of mucus from the airways, which impedes ventilation and leads to alveolar damage.[24] Qigong exercise comprises abdominal breathing and pursed-lip breathing, which can slow the breathing rate and improve the patient's breathing difficulties.[20] During the pronunciation of the 6 different sounds, the corresponding movement of the upper limbs not only increases the volume of the chest cavity and deepens breathing[25] but may also help to loosen the adhesion of mucus to the epithelium of the respiratory tract. In addition, many studies have shown that applying

Table 2
The changes in primary and secondary outcomes from pretreatment to discharge

Outcome	QARP group (n=64)			Standard therapies group (n=64)			Between-group difference (95% CI)	P
	Pre	Post	Difference	Pre	Post	Difference		
mMRC	2.9 (2.7, 3.1)	1.0 (0.9, 1.1)	-1.8 (-2.1, 1.6)*	2.7 (2.5, 2.8)	1.1 (1.0, 1.3)	-1.5 (-1.7, 1.3)*	-0.3 (-0.6, 0.1)*	0.018
MBS	5.5 (4.9, 6.1)	1.7 (1.5, 1.9)	-3.7 (-4.3, 3.2)*	5.3 (4.8, 5.8)	2.3 (1.9, 2.6)	-3.1 (-3.5, 2.6)*	-0.7 (-1.3, 0.0)*	0.045
FS-14	7.6 (6.8, 8.4)	3.8 (3.2, 4.4)	-3.8 (-4.8, 2.8)*	7.2 (6.6, 7.9)	3.5 (2.9, 4.0)	-3.8 (-4.7, 2.9)*	-0.03 (-0.7, 0.7)	0.931
PHQ-9	13.3 (12.0, 14.7)	7.1 (6.2, 8.0)	-6.5 (-8.1, 5.0)*	13.7 (12.3, 15.0)	6.6 (5.6, 7.6)	-7.0 (-8.7, 5.4)*	0.5 (-1.0, 2.1)	0.492
Temperature,℃	37.5 (37.3, 37.8)	36.5 (36.4, 36.6)	-1.0 (-1.3, -0.8) *	37.4 (37.2, 37.6)	36.5 (36.4, 36.5)	-0.9 (-1.1, -0.7)*	0.0 (-0.08, 0.09)	0.914
Heart rate (bpm)	85.5 (82.7, 88.4)	81.2 (79.4, 83.0)	-4.4 (-7.7, -1.0)*	85.4 (82.3, 88.5)	80.7 (78.0, 83.3)	-4.7 (-8.8, -0.7)*	0.3 (-2.6, 3.6)	0.754
Respiration rate (times/min)	23.1 (20.6, 25.6)	19.9 (19.6, 20.3)	-3.1 (-5.6, -0.6) *	22.6 (21.6, 23.6)	21.9 (19.8, 24.0)	-1.7 (-3.0, 1.5)*	-1.4 (-4.2, 1.3)	0.301
Systolic blood pressure (mmHg)	124.2 (121.9, 126.6)	120.3 (117.8, 122.8)	-3.9 (- 7.3, -0.5)*	123.3 (119.9, 126.6)	123.6 (121.0, 126.3)	0.3 (- 3.9, 4.6)	-4.2 (-9.4, -0.9)	0.108
Diastolic blood pressure (mmHg)	73.0 (70.7, 75.3)	73.2 (71.2, 75.2)	0.3 (-2.8, 3.3)	72.5 (70.2, 74.9)	74.0 (71.8, 76.1)	1.4 (-1.7, 4.6)	-1.1 (-4.9, 2.6)	0.537
Blood oxygen saturation (SaO_2)	92.7 (92.1, 93.2)	97.0 (96.5, 97.4)	4.3 (3.6, 5.0)*	92.8 (92.1, 93.5)	97.0 (96.4, 97.6)	4.2 (3.3, 5.1)*	0.0 (-0.8, 0.7)	0.967

*, $p<0.05$. MBS, modified Borg dyspnea scale; FS-14, Fatigue Scale-14; PHQ-9, Patient Health Questionnaire-9 scale; mMRC, Medical Research Council; QARP, Qigong exercise and acupressure telerehabilitation program; SaO2, oxygen saturation; COVID-19, coronavirus disease of 2019; CI, confidence intervals.

Table 3
Hospital days and duration of symptom disappearance after treatment.

Symptom	Hospital days and duration of symptom disappearance (days)		Between-group difference	
	QARP group (n=64)	Standard therapies group (n=64)	QARP group vs. Standard therapies group	*p value*
Hospital days	18.5 (17.0, 20.0)	20.8 (19.2, 22.3)	-2.2 (-4.4, -0.1) *	0.042
Cough	14.3 (12.6, 16.1)	17.0 (15.0, 19.1)	-2.7 (-5.4, -0.1)*	0.046
Fever	5.9 (4.7, 7.1)	6.3 (4.9, 7.6)	-0.3 (-2.1, 1.4)	0.710
Dyspnea	10.2 (8.4, 12.0)	10.6 (8.1, 13.0)	-0.4 (-3.4, 2.7)	0.814
Diarrhea	3.4 (2.5, 4.3)	4.4 (2.7, 6.2)	-1.0 (-3.0, 0.9)	0.285
Fatigue	8.4 (6.8, 10.0)	10.4 (8.0, 12.8)	-2.0 (-4.9, 0.9)	0.174

Values are expressed as mean (95% confidence intervals). $^{*}p < 0.05$, a significant difference was found between the two groups. QARP, Qigong exercise and acupressure telerehabilitation program.

pressure on acupoints related to the lungs helps improve dyspnea.[26-28] The QARP group had a significantly reduced cough duration, which may be related to the specific acupoints selected for this study (Feishu, Danzhong, and Zhongfu), all of which are related to relieving cough.[29] Previous studies have shown that qigong exercise and acupressure can improve the patient's symptoms of fatigue and anxiety.[23,30] However, we did not observe significant differences in FS-14 and PHQ-9 scores between the two groups, probably due to the relatively short duration of the intervention and the selection of acupoints related to relief of dyspnea and cough rather than to other specific outcomes.

4.4. Implications for clinical practice and future studies

Because of its simplicity, therapists can also remotely instruct patients to practice qigong exercise online. Research has shown that telerehabilitation can avoid hospital-acquired infections, reduce the use of personal protective equipment, and be safe and effective.[31] Telerehabilitation is suitable for the early-stage rehabilitation of patients with severe COVID-19. At present, QARP plus standard therapies is a new integrative therapy, and more large-sample clinical studies are needed to prove its efficacy in patients with severe COVID-19.

4.5. Limitations of the study

Our study has some limitations. First, the observation time was short, and data were only recorded during the patients' stay in the hospital. Therefore, it is necessary to further study the long-term clinical efficacy of QARP for severe COVID-19. Second, during our trial design, it was difficult to assess patients purely for COVID-19 because they had comorbidities, and although we used a randomized grouping approach, some bias was unavoidable.

4.6. Conclusion

This study showed that QARP plus standard therapies may help improve lung function and symptoms such as shortness of breath and cough and reduce the length of hospital stay. Therefore, QARP plus standard therapies may be an option for patients with severe COVID-19.

Author contributions

Conceptualization: LF. Methodology: LF. Investigation: XF and WC. Formal Analysis: S-TL, Y-JM, CZ, and CG. Writing – Original Draft: S-TL, Y-JM, and CZ. Writing – Review and Editing: LF. Supervision: LF. All the authors have read and approved the final version of the manuscript.

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Conflict of interest

The authors declare that they have no conflicts of interest.

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Ethical statement

This RCT was approved by the Ethics Committee of Huangshi Hospital of Traditional Chinese Medicine (item number: HSZYYJ-2020-003-01). Informed consent was obtained from all participants.

Data availability

The data will be available on request from the corresponding author.

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