Research Article

Efficacy of Acupuncture Combined with Rehabilitation Training for Intensive Care Unit-Acquired Muscle Weakness: A Protocol for a Randomized, Sham-Procedure-Controlled Clinical Trial

Yin Shou,1 Wei Jin,2 Lingling Zhuang,3 Chenxia Xue,4 Li Hu,5 Siwei Xu,1 Kaiyong Zhang,1 Huiru Jiang,1 Peng Liu,1 and Bimeng Zhang

1Department of Acupuncture-Moxibustion, Shanghai General Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China
2Department of Critical Care Medicine, Shanghai General Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China
3Department of Ultrasound Medicine, Shanghai General Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China
4Department of Rehabilitation Medicine, Shanghai General Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China
5Acumox and Tuina Research Section, College of Acumox and Tuina, Shanghai University of Traditional Chinese Medicine, Shanghai, China

Correspondence should be addressed to Bimeng Zhang; acusc2007@126.com

Received 7 June 2021; Accepted 22 September 2021; Published 20 October 2021

Academic Editor: Talha Bin Emran

Copyright © 2021 Yin Shou et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

To evaluate the efficacy of acupuncture combined with rehabilitation training in patients with intensive care unit (ICU)-acquired muscle weakness (ICUAW), a single-blinded, randomized, sham-controlled clinical trial is designed for execution. In total, 56 participants with ICUAW will be randomly assigned to the treatment and control groups with 28 participants in each group. The participants will be treated with acupuncture or sham procedures at LI15, LI11, ST36, GB34, and ST31, 5 times per week for a total of 20 sessions in 4 weeks while they will receive rehabilitation training. Patients will be followed up every month for 3 months after treatment. The primary outcomes include changes in quadriceps femorius muscle area, thickness, vastus intermedius muscle thickness, subcutaneous tissue thickness, and ultrasonic intensities of the rectus femoris. The secondary outcomes consist of the modified Barthel index score and the Medical Research Council total score. Participants’ mechanical ventilation, the rate of detachment at the second week, the 28-day survival rate, and the occurrence of adverse reactions will be measured, and any side effects will be reported and recorded. Patient outcomes between the treatment and control groups will be compared and statistically tested. We anticipate that the therapeutic regimen of acupuncture combined with rehabilitation training would be more effective than the rehabilitation training alone for the treatment of the ICUAW. The findings of this study could help develop a better strategy for the treatment of the ICUAW disease and explore a clinical application of an acupuncture technique. Trial registration: Chinese Clinical Trial Register ChiCTR2000038779. Registered 30 September, 2020, https://www.chictr.org.cn/showproj.aspx?proj=62284.
1. Introduction
The intensive care unit (ICU)-acquired weakness (ICUAW) is a generalized muscle weakness complication developed during ICU admissions for which no other disease cause can be identified except for acute illness or its treatment. Approximately 40% of ICU patients with a history of at least 48 h of mechanical ventilation develop ICUAW. The disease affects peripheral and respiratory muscles, causing prolonged time of mechanical ventilation and hospital stay, increased hospital mortality, and chronic disability [1–5]. The mechanisms by which ICUAW develops are complex and involve functional and structural alterations in both the muscles and the nerves. Recovery from ICUAW typically takes several weeks or months, and muscle weakness in some patients can last for up to 2 years after discharge from the ICU. Because the pathogenesis of ICUAW is still unclear, there are no specific treatments. The current management of ICUAW includes an active treatment of the primary disease (e.g., sepsis), prevention of infection, control of high blood sugar, reduction of the duration of immobilization, and avoidance of other known risk factors, such as malnutrition, unnecessary application of corticosteroids and neuromuscular blockers, and early rehabilitation [6–8]. Thus, the development of easy-to-perform, more effective ICUAW-targeted interventions is needed for the prevention and treatment of ICUAW.

Acupuncture is a component of the traditional Chinese medicine that is practiced in China as well as abroad as a part of medical care for systemic disease treatment and is believed to work on the principle of the redistribution of “QI,” the life energy concept in Chinese. As per traditional Chinese medicine, diseases result from an imbalance or poor flow of QI. Acupuncture can cure the diseases based on the conduction of meridians and acupoints and following the application of certain operations to improve the flow of QI. In our previous studies, we found that ICU-acquired myasthenia is an acute polymyopathy, and early rehabilitation exercise alone can only reduce physiological dysfunction. Based on our clinical experience on the treatment of various neuromyopathy diseases, we found that acupuncture therapy can improve patients’ nerve function [9], restore their muscle atrophy [10] and muscle mass and strength [11], relieve their symptoms, shorten offline time and hospital stay, and improve the quality of patients’ lives. In particular, it can significantly alleviate the obvious atrophy of lower limb muscle thickness and cross-sectional area of ICU patients with acquired muscle weakness [12, 13]. More recent studies have found that the combination of acupuncture and speech rehabilitation training improved the total response rate of stroke patients with dysarthria [14]. Based on these studies, we presume that acupuncture and moxibustion combined with rehabilitation training can synergize the effects and offer complementary advantages. The combined therapeutic strategy is superior to simple acupuncture and rehabilitation training alone for the prevention and treatment of patients with ICUAW. However, the efficacy of this therapeutic regimen has not been evaluated yet. To test this hypothesis, we designed a randomized controlled trial with a 3-month follow-up to evaluate whether acupuncture combined with rehabilitation training benefits the recovery of patients with ICUAW and planned to determine the temporal extent of this effect after last successful treatment.

2. Methods and Analysis

2.1. Design. A parallel-group, randomized, and single-blinded (outcome assessors) prospective clinical trial was designed according to the Consolidated Standards of Reporting Trials (CONSORT 2010) guidelines (Figure 1), Standards for Reporting Interventions in Controlled Trials of Acupuncture (STRICTA) [15, 16], and Standard Protocol Items—Recommendations for Interventional Trials (SPIRIT) statement (Figure 2) [17] and the SPIRIT checklist. Patients with ICUAW will be recruited from the Shanghai General Hospital, which is affiliated to the Shanghai Jiaotong University from October 2020 to September 2023. Participants will be screened based on the inclusion and exclusion criteria; briefed on the purpose, procedures, treatments, and possible risks of the trial; and informed of their rights to discontinue participation in the clinical study at any time point. Once participants will have signed the written consent forms, they will receive either 20 sessions of acupuncture plus rehabilitation training therapy or sham acupuncture plus rehabilitation training for 4 weeks. The study design flow chart and the schedule are presented in Figure 1 and Table 1, respectively. In this study, we will follow the methods of Shou et al. 2020 [18].

2.2. Modified Barthel Index (MBI) Score and Medical Research Council (MRC) Total Score

2.2.1. Inclusion Criteria. Participants who would meet all of the following criteria will be enrolled in the study: (1) age >18 years, male and female patients diagnosed with ICUAW; (2) those who were previously admitted to ICU for more than 24 h; (3) acute physiology and chronic health disease classification system II (APACHEII) scores in the range of 8–20 points calculated based on the 12 admission physiologic variables and patient’s age and chronic health, as described by Knaus et al. [19]; (4) patients with stable hemodynamics; (5) patients with mechanical ventilation, oxygen concentration [fraction of inspired oxygen (FiO2)] < 0.6, and positive end-expiratory pressure (PEEP) < 10 cmH2O; and (6) patients who would either themselves and/or their families voluntarily agree to participate in the study and provide signed informed consent.

2.2.2. Exclusion Criteria. ICUAW patients who have or had suffered from any of the following conditions will be excluded from the study: (1) primary neurological and muscular diseases before admission, including brain and spinal cord injury, Guillain–Barre syndrome (GBS), and myasthenia gravis; (2) limb disability and limb instability fracture; (3) malignant tumors; (4) active bleeding; or (5) alcoholic patients who would not stop drinking during the trial.
2.2.3. Elimination Criteria. Enrolled participants will be allowed to withdraw from the study after being subjected to the assigned treatment if they: (1) leave the clinical trial for any personal reasons, (2) experience severe adverse life events that require them to withdraw from the trial, (3) do not fully participate in the treatment or follow-ups, and (4) do not comply with the treatment or fail to provide the information required for evaluation.

2.2.4. Ethics. The study was approved by the Ethics Committee of the Institute of Shanghai General Hospital, which is affiliated to the Shanghai Jiaotong University [(2020)98]. An informed consent form will be prepared and provided to the participants for obtaining their signatures (as stated earlier).

2.2.5. Randomization and Blinding. Participants will be randomly assigned (in a 1:1 ratio) to either the treatment group or the control group based on blocked randomization using a randomization table. The table will contain, in a random order, all possible combinations of a small series of figures and assume that patients are randomly assigned to treatment or control groups with equal probability. The

---

**Figure 1**: Flow chart of the study design.

**Figure 2**: Total study period and evaluation time points.
order of the interventions assigned to each block will be randomized. The process will be repeated for consecutive blocks until all participants would have been randomized. During the period when the participants will receive the first treatment, they will be given sequential treatment cards from independent researchers to ensure adequate concealment. All participants will be treated separately to prevent communication. Except for acupuncturists, all relevant parties will be blinded to the intervention groups. The implementation of treatments will be performed by two acupuncturists who will use patches prepared by operational assistants. The needles will be applied to every participant in the treatment and control groups. In addition, acupuncturists, operational assistants, and research nurses will be instructed to refrain from communicating with the participants regarding anything that would lead them to determine their group allocation. In addition, outcome evaluators and statistical analysts will be blinded and will not be involved in any part of the design and treatments during the trial.

2.2.6. Acupuncture and Sham Therapy. All research assistants and licensed acupuncturists involved in the trial will receive a 2-day training prior to the onset of the study. Both treatments will consist of 20 sessions over 4 weeks, 5 times per week, and each for 30 min. We plan to treat the patients for 4 weeks because normally our patients would have stayed in ICU for 4 weeks. Briefly, patients will be asked to lie down in a supine position. After sterilization, the 0.25 x 40 mm acupuncture needles (Suzhou Tianxie Acupuncture Instruments Co., Ltd., Suzhou, China) will be inserted to the acupoints of the Jianyu (LI15), Quchi (LI11), Zusanli (ST36), Yanglingquan (GB34), and Biguan (ST31) using a neutral reinforcing and reduced manipulation technique. Each needle will be rotated until the patient experiences the "QI" feeling of soreness, heaviness, and the sensation of distension. The procedure for conducting will be standardized as shown in Table 2. Participants in the control group will receive sham needling at the same acupoints with nested blunt needles. All the procedures will remain the same as the one in the treatment group with the exception of the needles, which will be forced to pierce the fixed pad and reach the skin surface without penetrating the skin. All participants will receive regular rehabilitation training.

2.3. Health Education. The conscious participants will be explained about the condition and their current situations, encouraged to have a positive attitude, and will be provided timely feedback on the stability of their vital signs. We plan to divert their attention, arrange visits from their family members, solve their psychological barriers, and eliminate their fears.

2.4. Rehabilitation Training

2.4.1. Strategy. Physicians will first assess the tolerance of the patients to rehabilitation treatment. They will repeatedly evaluate whether the patients’ oxygen supplies meet the respective consumptions and the conditions of their neurological, respiratory, circulatory, and other systems to determine the exercise mode of rehabilitation. Generally, rehabilitation intervention will be conducted in accordance with the following conditions: (a) maintenance of response to stimulation, having measurable cognitive ability characteristics, understanding of certain commands such as those that instruct them to open/close their eyes, look at people, show their tongues, nod, frown, and others; (b) FiO\textsubscript{2} < 60%, PEEP < 10 cmH\textsubscript{2}O; and (c) lack of orthostatic hypotension symptoms or need to pump vasoactive drugs. All patients will be required to be free of deep-vein thrombosis.
2.10. Outcome Measures

2.10.1. Baseline Information. Demographic information will be collected using a custom-made, standardized survey form that includes center location, name, age, gender, address, telephone number, and employment. Medical information will be collected using a custom-made form that records clinical information, including diagnosis, medication history, and APACHEII rating forms.
2.11. Primary Outcome Measures. The average change in the quadriceps femoris muscle area, thickness, vastus intermediate muscle thickness, subcutaneous tissue thickness, and ultrasonic intensity of the rectus femoris will be measured in a blinded manner, and the scores obtained at the baseline and at the end of the 4-week treatment will be compared for each group.

2.12. Secondary Outcome Measures. The average change in quadriceps femoris muscle area, thickness, vastus intermediate muscle thickness, subcutaneous tissue thickness, and ultrasonic intensity of the rectus femoris will be measured, and the scores obtained at the baseline, 2 weeks, and 3 months after the last treatment will be compared. MBI and MRC scores will be evaluated at 2 weeks, 4 weeks, and 3 months after the last treatment. The participants’ mechanical ventilation, rate of detachment at the second week, 28-day survival rate, and occurrence of adverse reactions will be evaluated, and any noticed side effects of the treatment will be recorded. All outcome readings will be scored on quantitative scales and presented as mean values and standard deviations.

2.13. Safety Assessment. Adverse events (AEs) are defined as events in which at least four participants suffer from the same symptom, including any undesirable experiences that may occur during the trial period. This may or may not be associated with the intervention. Participants will be instructed to report any AE to the research team at any time. All details of AE, including the time of occurrence, description of symptoms, duration of symptoms, severity, management measures, and causality to the intervention, will be recorded on case report forms (CRFs). The common AEs related to acupuncture, including local skin pain, itching, ulcers, leaving needles in participants, nausea during acupuncture, fainting during acupuncture, severe sharp pain, sharp pain lasting for more than 30 min, hematomas around the site of needling, bleeding, numbness, infection around the needle sites, sleeplessness after acupuncture, and dizziness after acupuncture, will be reported [20]. The causality between AEs and intervention will be assessed according to the World’s Health Organization Uppsala Monitoring Center System for Standardized Case Causality Assessment [21]. In the event of AE occurrence, patients will be given an appropriate treatment until their conditions stabilize. Severe AEs will be reported to the safety monitoring board within 24 h.

2.14. Follow-Up. The health statuses of the participants after the 4-week treatment period will be followed up on a monthly basis via telephonic and message communications for 3 months based on the previous study for this disease [22]. The symptoms and medication compliance or changes in medication will be recorded. In the event that participants withdrew from the trial or deviated from the intervention protocols, the staff will record the reasons for their withdrawal and the details of their new medications as well as the latest outcome data including the symptoms and frequency of the attacks prior to their exclusion from the study.

2.15. Participant Timeline. An overview of the recruitment timeline, interventions, and all time points of participant evaluation is summarized in Figure 2.

2.16. Data Collection and Management. The study staff will be responsible for the collection of baseline characteristic data and medical results during the screening period. All participants’ scores, observation times, AE records, and safety assessments will be consolidated in a single CRF. CRFs will be filled out immediately and accurately. Outcome evaluators will examine the outcomes at the baseline (before the treatment), 2 weeks (during the treatment), 4 weeks (end of treatment), and 3 months after last treatment (during the follow-up period). Data monitoring and management will be performed every 3 months by the Clinical Research Center of the Shanghai General Hospital affiliated to the Shanghai Jiaotong University. The clinical research monitors will monitor the medical practitioners to ensure that all processes are implemented correctly. A data monitoring committee (DMC) independent of the sponsor and with no conflicts of interest will be responsible for monitoring the progression of the trial and ensuring patient safety. Interim analyses and trial discontinuation plans will not be specified, but will be provided upon DMC’s request. Two assistants will enter all the data in an electronic database based on double data entry. The statistical manager will be responsible for data organization, coding, range checks for data values, and data conversion for quality control. The database will be locked after cleaning all data. If any participant withdraws from the trial, detailed reasons will be collected, and the rate of withdrawal will be analyzed statistically.

2.17. Quality Control. All the staff involved in the study, including acupuncturists, rehabilitation therapists, ultrasound examination doctors, operational assistants, and nurses, will be obliged to receive advanced training on filling out CRFs, conducting blood tests, details of acupuncture and rehabilitation therapy, scales and ultrasound examinations, and follow-up visit skills. All the staff members will be asked to take exams after training to ensure strict adherence to the study protocol and consistency of the trial administration processing, including acupuncture, rehabilitation therapy, and evaluation methods. All the staff members will be provided with a written protocol and standard operation procedure documents. All acupuncturists have acquired acupuncture licenses from the Ministry of Health of People’s Republic of China; they must have a clinical experience of >5 years. To improve the quality of study reporting and conduct, we will develop a standard operating procedure manual according to the principles of the Consolidated Standards of Reporting Trials Extension for Chinese Herbal Medicine Formulas [23]; it will be explained to all the investigators. Intervention details, such as acupuncture
2.18. Statistical Analysis

2.18.1. Sample Size Calculation. The trial will test two groups in parallel. The sample size calculation will be performed using the software SAS (version 9.3, SAS Institute Inc., Cary, NC, USA). The mean change in the primary outcome before and after treatment will be used as the indicator of efficacy evaluation in the calculation of the sample size. The results of previous studies yielded a mean ultrasound measurement of muscle thickness change of \(0.45 \pm 0.1\) [25] and a mean ultrasonic intensity of muscle change of \(25 \pm 3\) [26] after the loss of muscle mass and function. To detect a significant difference with a power of 80%, an alpha value of 0.05, and an acceptable delta value of 0.2, a sample size comprising at least 23 participants in each group will be needed. We have added an additional five patients per group considering a possible 20% dropout.

2.18.2. Software for Statistical Analyses. Statistical analysis will be performed using SPSS (version 26.0, SPSS Inc., Chicago, IL, USA) in the Clinical Evaluation Center of Shanghai General Hospital, which is affiliated to the Shanghai Jiaotong University.

2.19. Sample Distribution. The size and dropout rate of each data set will be described. Detailed reasons related to participants’ withdrawal from the trial will be provided.

2.20. Baseline Information. Baseline-adjusted analyses will be conducted for center and severity variables, and the baseline value of the corresponding outcomes will be assessed. Descriptive statistics will be used to compare baseline measures with participant characteristics. If an imbalance occurs in the baseline characteristics between the two groups, the analysis of variance will be applied.

2.21. Efficacy Analysis. Efficacy data analyses will be conducted based on the intention-to-treat population. All participants will be initially included in one of the two groups and considered in the statistical analyses. Analysis of efficacy will be conducted for each protocol and include all the participants who would complete the entire research processing. Descriptive statistics will be used to report primary outcome indicators between the two groups. All the data will be statistically analyzed using SPSS. All measurements will be expressed as mean ± standard deviation. The \(t\)-test will be used for comparisons between two samples if the distributions are normal, and the \(F\)-test will be used for comparisons among multiple samples. The Kruskal–Wallis \(H\)-rank sum test was used if the distribution is not normal. The participants’ sex and course of disease will be recorded, and the data will be tested using the \(\chi^2\) test. The ultrasound data will be analyzed by a mixed-effect model. The Cox-regression analysis will be performed to identify outcome-related factors. \(P < 0.05\) will be considered as statistically significant.

2.22. Safety Analysis. According to the definition of AEs, AEs will be recorded in conjunction with their severity level, causes, and explanations. Moreover, the number and the rate of AE will be described statistically. If AEs would be required to be compared between groups, the \(\chi^2\) test or the Fisher’s exact test will be used for statistical analyses.

2.23. Missing Data Analysis. All data used in the main statistical analyses will be collected by the fourth week of the treatment and end of the 3-month follow-up period. If any of the data are not obtained, the assumed missing data mechanism will be analyzed, and a multiple adjustment approach will be used. After the main analysis, a sensitivity analysis will be performed for the various data sets to enable an assessment of the impact of the missing data on the results. A fully specified statistical analysis plan will be written independently.

2.24. Publication and Dissemination. Following the completion of data analyses, Chinese and English language disseminations will be planned. Trial results will be disseminated via conferences or publications. No public access will be provided to the entire protocol, participant data sets, or statistical code. However, scientists will be able to gain access to the full protocol through the Ethics Committee of the Institute of Shanghai General Hospital upon request. This protocol was written following the SPIRIT checklist. The future report will follow the CONSORT guidelines [13], revised STRICTA [12], and the extension of CONSORT for reporting single-blinded randomized trials.

3. Discussion

ICUAW is a frequent complication of critical illness, with devastating short- and long-term consequences. Therefore, effective prevention and/or treatment of ICUAW are required. Currently, the prevention of ICUAW development seems, at least in part, possible. However, to date, there is no effective therapeutic strategy to treat the disease [27, 28]. Some studies have shown that early rehabilitation has a positive effect on ICUAW recovery, shortens ICU and...
hospital stays, decreases the duration of mechanical ventilation, improves long-term functional independence, and reduces mortality [29–31]. However, a systematic review could not support the fact that post-ICU physical rehabilitation was beneficial because of the lack of high-quality data and existence of heterogeneity [32]. Another randomized controlled trial including 120 patients with acute respiratory failure found that the length of ICU and hospital stays were longer in the intervention group compared with those in the control group [33]. The early rehabilitation during ICU stay was not associated with improvements in functional status, muscle strength, quality of life, or healthcare utilization outcomes, although it seemed to improve walking ability compared with usual standard care [34,35]. Thus, additional studies are required to design new preventive and/or therapeutic strategies that can be tested in adequately powered, large-scaled, well-performed, randomized controlled trials. Therefore, we developed the protocol of a randomized controlled trial presented herein to assess the effectiveness and safety of acupuncture combined with rehabilitation training for the treatment of patients with ICUAW.

Acupuncture is a feasible, safe, and acceptable therapy in ICU settings for patients with diversity backgrounds [36]. The therapeutic advantage of using acupuncture as an adjuvant therapy lies in the fact that the combination benefits the respiration of ICU patients on ventilation machine and helps weaning from prolonged ventilation [37]. The application of transcutaneous electrical nerve stimulation on acupuncture points has been shown to decrease the level of pain and opioid consumption in intubated patients connected to mechanical ventilators [38]. In addition, combined therapy of acupuncture with herbal medicine has been found to reduce the incidence of delirium in patients with cardiovascular disease in ICUs [39]. Furthermore, it is known that acupuncture with oral administration of essential amino acids is more effective and the combination can increase muscle mass in a relatively shorter time than treatment with the essential amino acids alone [11]. Recent studies have demonstrated that acupuncture can counteract skeletal muscle atrophy by increasing IGF-1 levels and by stimulating muscle regeneration [40]. In this report, we designed a single-blinded, randomized, sham-procedure-controlled, clinical trial with a 3-month follow-up for the assessment of the efficacy of acupuncture combined with rehabilitation training in patients with ICUAW. Successful completion of the proposed clinical trial will provide strong evidence that the therapeutic regimen of acupuncture combined with rehabilitation training is more effective than the rehabilitation training alone for the treatment of the ICUAW. The findings of this study could help to develop a better strategy for the treatment of the ICUAW disease and expand the application of acupuncture technique in clinical settings.

In this study, we proposed the use of muscular ultrasonography to evaluate the muscle strength by visualizing the muscle’s cross-sectional area, layer thickness, and echo intensity based on the grayscale and penetration angle [41]. This is because the ultrasonic measurement of muscle thickness can be used to assess the presence of sarcopenia, and the echo intensity can be associated with muscle strength and correlated with the risk of frailty in elderly outpatients [25,26]. We believe that muscle ultrasound can reliably detect the pathological changes of ICUAW [41]. Our study will address whether this treatment will affect the quadriceps femoris muscle area, thickness, vastus intermedius muscle thickness, subcutaneous tissue thickness, ultrasonic intensity of the rectus femoris, and MBI and MRC total scores in the long term after the last treatment.

Data Availability
The data used to support the findings of this study will be available from the corresponding author upon request.

Disclosure
The Shanghai General Hospital Affiliated to Shanghai Jiaotong University has ownership of the data, but does not have rights to the interpretation of data or influence over the processes in this study.

Conflicts of Interest
The authors declare that there is no conflict of interest for the publication.

Acknowledgments
The authors acknowledge the Shanghai University of Traditional Chinese Medicine in Shanghai and Professor Pinxian Huang for her statistical support of this protocol. The authors also appreciate the technological support from the Shanghai Public Health Clinical Center, Fudan University, and Dr. Rong Chen. The authors also appreciate the cooperation of the participants in this trial. This study was supported by grants from the Shanghai Municipal Health Bureau (2020LP010, ZY(2018-2020)-FWTX-8008) and the National Natural Science Foundation of China (81403470).

References
[1] N. Latronico and C. F. Bolton, “Critical illness polyneuropathy and myopathy: a major cause of muscle weakness and paralysis,” The Lancet Neurology, vol. 10, no. 10, pp. 931–941, 2011.
[2] T. J. Loftus, F. A. Moore, and L. L. Moldawer, “ICU-acquired weakness, chronic critical illness, and the persistent inflammation-immunosuppression and catabolism syndrome,” Critical Care Medicine, vol. 45, no. 11, Article ID e1184, 2017.
[3] M. S. Herridge, A. M. Cheung, C. M. Tansey et al., “One-year outcomes in survivors of the acute respiratory distress syndrome,” New England Journal of Medicine, vol. 348, no. 8, pp. 683–693, 2003.
[4] W. D. Schewickert and J. Hall, “ICU-acquired weakness,” Chest, vol. 131, no. 5, pp. 1541–1549, 2007.
[5] R. D. Stevens, D. W. Dowdy, R. K. Michaels, P. A. Mendez-Tellez, P. J. Pronovost, and D. M. Needham, “Neuromuscular dysfunction acquired in critical illness: a systematic review,” Intensive Care Medicine, vol. 33, no. 11, pp. 1876–1891, 2007.
[6] R. D. Zorowitz, “ICU-acquired weakness,” Chest, vol. 150, no. 4, pp. 966–971, 2016.
Evidence-Based Complementary and Alternative Medicine

[7] E. Fan, F. Cheek, L. Chlan et al., “An official American Thoracic Society Clinical Practice guideline: the diagnosis of intensive care unit-acquired weakness in adults,” *American Journal of Respiratory and Critical Care Medicine*, vol. 190, no. 12, pp. 1437–1446, 2014.

[8] W. Q. Ma and M. J. Pu, “Research progress in Pathogenesis of ICU-Acquired weakness,” *Chinese Journal of Geriatric Care*, vol. 16, no. 3, pp. 118–119, 2018.

[9] J.-G. Song, H.-H. Li, Y.-F. Cao et al., “Electroacupuncture improves survival in rats with lethal endotoxemia via the autonomic nervous system,” *Anesthesiology*, vol. 116, no. 2, pp. 406–414, 2012.

[10] Z. Su, L. Hu, and J. Cheng, “Acupuncture plus low-frequency electrical stimulation (Acu-LFES) attenuates denervation-induced muscle atrophy,” *Journal of Applied Physiology*, vol. 120, no. 4, pp. 426–436, 2016.

[11] X. Zhou, B. Xing, G. He, X. Lyu, and Y. Zeng, “The effects of electrical acupuncture and essential amino acid supplementation on sarcopenic obesity in male older adults: a randomized control study,” *Obesity Facts*, vol. 11, no. 4, pp. 327–334, 2018.

[12] X. Li and C. X. Xiao, “Clinical study on electroacupuncture treatment of ICU acquired myasthenia gravis,” *Shandong Journal of Traditional Chinese Medicine*, vol. 37, pp. 560–562, 2018.

[13] W. M. Shang, T. Ma, C. Cheng, F. Wang, F. Hu, and M. Y. Yang, “Effect of electroacupuncture point stimulation combined with joint loosening training on the incidence of sexual failure in critically ill patients in intensive care unit,” *HuBei Journal of Traditional Chinese Medicine*, vol. 39, no. 9, pp. 44–46, 2017.

[14] Q. Xie, X. Chen, J. Xiao et al., “Acupuncture combined with speech rehabilitation training for post-stroke dysarthria: a systematic review and meta-analysis of randomized controlled trials,” *Integrative Medicine Research*, vol. 9, no. 4, Article ID 100431, 2020.

[15] K. F. Schulz, D. G. Altman, and D. Moher, “CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials,” *PLoS Medicine*, vol. 7, no. 3, Article ID e1000251, 2010.

[16] H. MacPherson and D. G. Altman, “Improving the quality of reporting acupuncture interventions: describing the collaboration between STRICTA, CONSORT and the Chinese Cochrane Centre,” *Journal of Evidence-Based Medicine*, vol. 2, no. 1, pp. 57–60, 2009.

[17] A.-W. Chan, J. M. Tetzlaff, P. C. Gotzsche et al., “SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials,” *BMJ*, vol. 346, Article ID e7586, 2013.

[18] Y. Shou, L. Hu, C. Zhang et al., “Efficacy of acupuncture at three nasal acupoints plus acupoint application for perennial allergic rhinitis: a multicenter, randomized controlled trial protocol,” *Trials*, vol. 21, no. 1, p. 110, 2020.

[19] W. A. Knaus, E. A. Draper, D. P. Wagner, and J. E. Zimmerman, “APACHE II: a severity of disease classification system,” *Critical Care Medicine*, vol. 13, no. 10, pp. 818–829, 1985.

[20] Z. Liu, S. Yan, J. Wu et al., “Acupuncture for chronic severe functional constipation: a randomized trial,” *Annals of Internal Medicine*, vol. 165, no. 11, pp. 761–769, 2016.

[21] J. P. Mouton, U. Mehta, D. P. Rossiter, G. Maartens, and K. Cohen, “Inter-rater agreement of two adverse drug reaction causality assessment methods: a randomised comparison of the liverpool adverse drug reaction causality assessment tool and the World health organization-uptsala monitoring centre system,” *PLoS one*, vol. 12, no. 2, Article ID e0172830, 2017.

[22] N. E. Brummel, T. D. Girard, P. P. Pandharipande et al., “Prevalence and course of frailty in survivors of critical illness,” *Critical Care Medicine*, vol. 48, no. 10, pp. 1419–1426, 2020.

[23] C.-W. Cheng, T.-X. Wu, H.-C. Shang et al., “CONSORT extension for Chinese herbal medicine Formulas 2017: recommendations, explanation, and elaboration,” *Annals of Internal Medicine*, vol. 167, no. 2, pp. 112–121, 2017.

[24] H. MacPherson, D. G. Altman, R. Hammerschlag et al., “Revised STandards for reporting interventions in clinical trials of acupuncture (STRICTA): extending the CONSORT statement,” *Journal of Evidence-Based Medicine*, vol. 3, no. 3, pp. 140–155, 2010.

[25] K. Rustani, L. Kundisova, P. L. Capecci, N. Nante, and M. Bicchi, “Ultrasound measurement of rectus femoris muscle thickness as a quick screening test for sarcopenia assessment,” *Archives of Gerontology and Geriatrics*, vol. 83, pp. 151–154, 2019.

[26] R. Mirón Mombiela, F. Palacio de Castro, P. Moreno, and C. Borras, “Ultrasonic echo intensity as a new noninvasive in vivo biomarker of frailty,” *Journal of the American Geriatrics Society*, vol. 65, no. 12, pp. 2685–2690, 2017.

[27] I. Vanhorebeek, N. Latronico, and G. Van den Bergh, “ICU-acquired weakness,” *Intensive Care Medicine*, vol. 44, no. 4, pp. 637–653, 2020.

[28] M. C. Kizilarslanoglu, M. E. Kuyumcu, Y. Yesil, and M. Halil, “Sarcopenia in critically ill patients,” *Journal of Anesthesia*, vol. 30, no. 5, pp. 884–890, 2016.

[29] P. E. Morris, A. Goad, C. Thompson et al., “Early intensive care unit mobility therapy in the treatment of acute respiratory failure,” *Critical Care Medicine*, vol. 36, no. 8, pp. 2238–2243, 2008.

[30] P. Bailey, G. E. Thomsen, V. J. Spuhler et al., “Early activity is feasible and safe in respiratory failure patients,” *Critical Care Medicine*, vol. 35, no. 1, pp. 139–145, 2007.

[31] D. M. Needham, “Mobilizing patients in the intensive care unit,” *Jama*, vol. 300, no. 14, pp. 1685–1690, 2008.

[32] B. Connolly, L. Salisbury, B. O’Neill et al., “Exercise rehabilitation following intensive care unit discharge for recovery from critical illness: executive summary of a Cochrane Collaboration systematic review,” *Journal of Cachexia, Sarcopenia and Muscle*, vol. 7, no. 5, pp. 520–526, 2016.

[33] M. Moss, A. Nordon-Craft, D. Malone et al., “A randomized trial of an intensive physical therapy program for patients with acute respiratory failure,” *American Journal of Respiratory and Critical Care Medicine*, vol. 193, no. 10, pp. 1101–1110, 2016.

[34] A. C. Castro-Avia, P. Serrón, E. Fan, M. Gaete, and S. Mickan, “Effect of early rehabilitation during intensive care unit stay on functional status: systematic review and meta-analysis,” *PLoS one*, vol. 10, no. 7, Article ID e0130722, 2015.

[35] K. Zang, B. Chen, M. Wang et al., “The effect of early mobilization in critically ill patients: a meta-analysis,” *Nursing in Critical Care*, vol. 25, no. 6, pp. 360–367, 2020.

[36] C. Feneen, E. Bruns, G. LeCompte, A. Forati, T. Chen, and A. Matecki, “Acupuncture for pain and nausea in the intensive care unit: a feasibility study in a public safety net hospital,” *Journal of Alternative & Complementary Medicine*, vol. 23, no. 12, pp. 996–1004, 2017.
in intensive care units: a retrospective observational study,” *Journal of Alternative & Complementary Medicine*, vol. 24, no. 11, pp. 1076–1084, 2018.

[38] J. AminiSaman, S. Mohammadi, H. Karimpour, B. Hemmatpour, H. Sharifi, and R. Kawyannejad, “Transcutaneous electrical nerve stimulation at the acupuncture points to relieve pain of patients under mechanical ventilation: a randomized controlled study,” *Journal of Acupuncture and Meridian Studies*, vol. 11, no. 5, pp. 290–295, 2018.

[39] J. Matsumoto-Miyazaki, H. Ushikoshi, and S. Miyata, “Acupuncture and traditional herbal medicine therapy prevent delirium in patients with cardiovascular disease in intensive care units,” *American Journal of Chinese Medicine*, vol. 45, no. 2, pp. 255–268, 2017.

[40] Z. Su, A. Robinson, L. Hu et al., “Acupuncture plus low-frequency electrical stimulation (Acu-LFES) attenuates diabetic myopathy by enhancing muscle regeneration,” *PloS one*, vol. 10, no. 7, Article ID e0134511, 2015.

[41] P. Formenti, M. Umbrello, S. Coppola, S. Froio, and D. Chiumello, “Clinical review: peripheral muscular ultrasound in the ICU,” *Annals of Intensive Care*, vol. 9, no. 1, p. 57, 2019.