



The effect of acupoint application of traditional Chinese medicine for the treatment of chronic obstructive pulmonary disease

A protocol for systematic review and meta-analysis

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Abstract

Background: Chronic obstructive pulmonary disease (COPD) is a public threat, leading to progressive physical activity and poor quality of life. Although modern medicine has excellent achievement of COPD, the recurrence rate of stable COPD and the mortality of acute exacerbation COPD remain high. As one of the external therapy of traditional Chinese medicine, acupoint application has been treated COPD in China for a long time. Nevertheless, study evaluating the effect of acupoint application for COPD could not satisfy needs for clinic.

Method: Randomized controlled trials meeting the inclusion criteria will be collected by the 2 reviewers. We choose the following electronic databases of Web of Science, Pub Med, EMBASE, Cochrane Library, China National Knowledge Infrastructure, Wan Fang, Chinese Scientific Journals Database, and Chinese Biomedical Database as our retrieval tool. The retrieval time was from inception to March 2020. The key to evaluation criteria is total clinical efficacy rate and lung function will be measured. Secondary outcomes include assessment scales and adverse reactions. The studies extracted will be assessed. The merging analysis will be carried out by Review Manager Software.

Result: A scientific evidence of efficacy and safety of acupoint application for COPD will be found.

Conclusion: The evaluation of the efficacy and safety of acupoint application for COPD will be presented.

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Abbreviations: AECOPD = acute exacerbation COPD, COPD = chronic obstructive pulmonary disease, TCM = traditional Chinese medicine.

Keywords: acupoint application, chronic obstructive pulmonary disease, protocol, systematic review

1. Introduction

Chronic obstructive pulmonary disease (COPD) is a common disease, characterized by persistent respiratory symptoms and airflow limitation and acute exacerbation. [1] Acute exacerbation COPD (AECOPD) occurs repeatedly, which brings about further aggravation of airway injury and the disease worsening. [2] The

clinical manifestations of COPD mainly represented as dyspnea, cough, expectoration, wheezing, and chest tightness. Hormone-reducing phlegm, cough medicines and long term domiciliary oxygen therapy usually are used for basic treatment, however, getting unsatisfactory effect. The prevalence of COPD is high, life security of patients is seriously affected. [3] With change of

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All data generated or analyzed during this study are included in this published article [and its supplementary information files].

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Liu et al. Medicine (2020) 99:43

environment and lifestyle, the incidence and mortality of COPD in the world increase every year, which has caused a significant social and economic burden. [4,5] Therefore, controlling the symptoms of stable COPD and reducing the number of AECOPD is critical issues which need to be solved.

Traditional Chinese medicine (TCM) has be used for treating plenty of acute and chronic diseases. [6-14] As one of the characteristic therapies of TCM external treatment, acupoint application also is widely recognized. [15] On the basic of the basic theory of TCM, acupoint application can be considered that the skin-related acupoints are stimulated through the penetration and pungent nature of Chinese herbal medicine, achieving the purpose of relieving symptoms and curing diseases. some studies have shown that acupoint application has a good clinical effect for COPD. [16] For patients with AECOPD, acupoint application can improve lung ventilation function, quality of life, and clinical symptoms. [17] For patients with stable COPD, acupoint application could also stabilize the COPD state of patients, relieve the clinical symptoms, and reduce the number of acute exacerbation. [18,19]

Acupoint application has the characteristics of simple operation, significant effect, and less adverse reactions, which has been widely recognized in the society. More and more researches about acupoint application for treating COPD were published. Therefore, reliable evidence will be required. The study will be adopted evidence-based medicine methods, objectively evaluating clinical efficacy and safety of acupoint application for COPD.

2. Method

2.1. Inclusion criteria

- **2.1.1.** *Types of study.* Inclusion: Whether they are blind or not, only clinical randomized controlled trial articles will be included of Chinese and English language. Exclusion: Animal experimental study and quasi-randomized trials will be excluded.
- **2.1.2. Study participants.** Diagnostic criteria: Patients who were diagnosed with COPD. Exclusion of severe cardiovascular, cerebrovascular diseases, and other complications. Exclusion of patients who are allergic to Chinese medicine application, or patients with skin rupture, hypersensitivity, or scar constitution.
- **2.1.3.** *Intervention.* Experimental group is conventional therapy combined with acupoint application regardless of herbal regimen, acupoints selected, patching time are eligible for inclusion. Control group is conventional therapy combined with placebo or not.
- **2.1.4. Outcomes.** Obvious efficiency, effective rate, and clinical control rate and lung function are primary outcomes. Assessment scales^[20] and adverse reactions are additional outcomes.

2.2. Search strategy

Qualified studies were extracted through literature search using Web of Science, Pub Med, EMBASE, Cochrane Library, China National Knowledge Infrastructure, Wan Fang, Chinese Scientific Journals Database, and Chinese Biomedical Database from inception to March 2020. And we also used references from previously published systematic reviews to manually search for relevant research. The following key search terms, including relative medical subject heading (Mesh) and free text term will be retrieved: "Chinese herbal medicine" or "traditional Chinese

medicine" or "TCM" or "acupoint application" or "Chinese acupoint application" or "Herbal medicine point application" or "Chronic obstructive pulmonary disease" or "COPD" or "acute exacerbation COPD" or "AECOPD" or "stable COPD."

2.3. Studies Selection

Two researchers (YF Liu and SQ Zeng) will independently scrutinize the headlines and resulting summaries to determine eligibility by pre-specified inclusion criteria independently. Disagreements are settled by consensus. A third reviewer will judge any discrepancies of inclusion article. Entire process will be proceeded in the preferred reporting item for systematic review and meta-analysis. [21] Figure 1 is the flow diagram.

2.4. Data extraction

Two researchers (YF Liu and SQ Zeng) will independently scrutinize the quality of inclusion studies, and discussion with a third reviewer will reach a consensus in case of discrepancy.

2.5. Risk of bias (quality) assessment

The study will be assessed through Cochrane Handbook for Systematic Reviews of Interventions. These indicators is categorized different risk of bias (including low, high, and unclear) if needed. The different opinion of 2 reviewers will be resolved by consultation with the corresponding authors.

2.6. Strategy for data synthesis

We will analyses results by Review Manager Software. For continuous outcomes, mean difference with 95% confidence intervals (Cist) will be usage. For dichotomous outcomes, risk ratio will be adopted. I^2 statistics will be used to assess heterogeneity. If no significant heterogeneity in the data (P > .05 and $I^2 < 50\%$), a fixed-effect model will be performed. If significant heterogeneity is found (P < .05 and $I^2 > 50\%$), a random-effects model will be conducted.

2.7. Analysis of subgroups or subsets

Clinical stage of acute exacerbation and stable will be carried out as 1 pre-specified subgroup analyses if possible.

2.8. Sensitivity analysis

If heterogeneity is significantly different, then sensitivity analysis method will be accepted for exploring it, based on Corresponding clinical parameters.

2.9. Ethics and dissemination

The work is intent to published in peer-reviewed journals. Ethical permission is not required because the research is systematic review through published data which excluded personal information of patients.

3. Discussion

COPD becomes the fourth cause of death around the world. In addition, the incidence has gradually increased. ^[22] In China, more than 1 million people died of COPD and more than 5

Liu et al. Medicine (2020) 99:43 www.md-journal.com

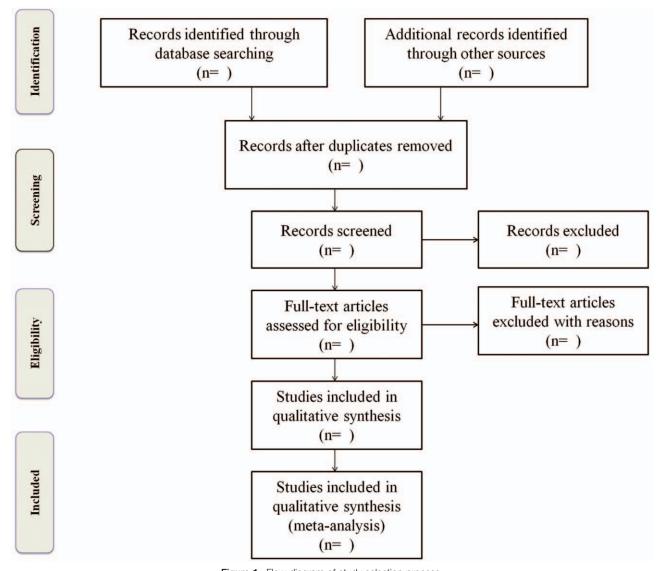


Figure 1. Flow diagram of study selection process.

million people are disabled per year. ^[23] COPD is closely related to factors such as respiratory infection, dust, chemical inhalation, and air pollution. Importantly, AECOPD is often caused by microbial infections, ^[23] which may induce complications such as respiratory failure and sleep-disordered breathing. ^[24–26] Acute exacerbation increases the difficulty of treating COPD.

COPD is commonly treated by using modern medicine such as bronchial relaxation, anti-inflammatory, anti-infection, ventilation support, expectoration, and nutritional support. Nevertheless, modern medicine is poor curative effect in improving the patient's respiratory endurance and quality of life. On the contrary, a certain degree of damage to the patient's body will be caused by long-term use of drugs or the continuous increase in drug doses. Therefore, it is necessary to find other effective treatment methods as adjuvant therapy for COPD.

High-quality preventive measures can reduce the progression of the disease for stable COPD which can be prevented the occurrence of acute exacerbation. Since 2015, the Global Initiative for Chronic Obstructive Pulmonary Disease pointed

out that lung rehabilitation has become increasing significant in the treatment for COPD. [29] Therefore, how to control the stable and reduce acute exacerbation is the top priority of the current treatment for COPD through pulmonary rehabilitation program.

As a treatment mean of pulmonary rehabilitation, acupoint application could play a critical role in prevention and treatment for diseases based on basic theory of TCM. In recent years, the efficacy of acupoint application for COPD has gradually been accepted. Acupoint application embodies the characteristic and advantage of TCM for "preventing disease." Acupoint application is an important part of the external treatment method of TCM. Simple and easy operation is the main characteristic of acupoint application.

In this systematic review and meta-analysis, we will accomplish a assessment of the efficacy and safety of acupoint application for COPD. This meta-analysis will be followed by a standard procedure such as preferred reporting item for systematic review and meta-analysis standard. We intend to provide a reliable evidence for clinical application of acupoint application.

Liu et al. Medicine (2020) 99:43

However, some limitations remain exist. For example, we only published related studies in English and Chinese, perhaps some publication bias may be occurred.

Author contributions

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Supervision: Yu Li. Validation: Yue Su.

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References

- [1] Singh D, Agusti A, Anzueto A, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive lung disease: the GOLD science committee report 2019. Eur Resp J 2019;53:12.
- [2] Yang IA, Browns JL, George J, et al. COPD-X Australian and New Zealand guidelines for the diagnosis and management of chronic obstructive pulmonary disease: 2017 update. Med J Aust 2017;207:436–42.
- [3] Gebrehiwot TT, Lopez AD. GBD 2015 Chronic Respiratory Disease CollaboratorsGlobal, regional, and national deaths, prevalence, disability-adjusted life years, and years lived with disability for chronic obstructive pulmonary disease and asthma, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015 (vol 5, pg 691, 2017). Lancet Resp Med 2017;5:E30–130.
- [4] Incidence GBDDIGlobal, regional, and national age-sex specific mortality for 264 causes of death, 1980-2016: a systematic analysis for the Global Burden of Disease Study 2016 (vol 390, pg 1211, 2017). Lancet 2017;390:E38–138.
- [5] Viinanen A, Lassenius MI, Toppila I, et al. The burden of chronic obstructive pulmonary disease (COPD) in Finland: impact of disease severity and eosinophil count on healthcare resource utilization. Int J Chronic Obstr Pulm Dis 2019;14:2409–21.
- [6] Li FS, Gao Z, Jing J, et al. Effect of point application on chronic obstructive pulmonary disease in stationary phase and effects on pulmonary function: a systematic evaluation of randomized controlled trials. J Tradit Chin Med 2012;32:502–14.
- [7] Wang L, Zheng XL, Hui Y, et al. Adjuvant treatment with Xiaoqinglong formula for bronchial asthma protocol of systematic review and metaanalysis. Medicine (Baltimore) 2019;98:4.
- [8] Chang CC, Chen TL, Chiu HE, et al. Outcomes after stroke in patients receiving adjuvant therapy with traditional Chinese medicine: a nationwide matched interventional cohort study. J Ethnopharmacol 2016;177:46–52.
- [9] Li SY, Li JS, Wang MH, et al. Effects of comprehensive therapy based on traditional Chinese medicine patterns in stable chronic obstructive pulmonary disease: a four-center, open-label, randomized, controlled study. BMC Complement Altern Med 2012;12:11.
- [10] Miller KR, Patel JN, Symanowski JT, et al. Acupuncture for cancer pain and symptom management in a palliative medicine clinic. Am J Hosp Palliat Med 2019;36:326–32.
- [11] Ni XJ, Shergis JL, Zhang AL, et al. Traditional use of chinese herbal medicine for insomnia and priorities setting of future clinical research. J Altern Complement Med 2019;25:8–15.

[12] Chen ZK, Wang XN, Li YY, et al. Comparative network pharmacology analysis of classical TCM prescriptions for chronic liver disease. Front Pharmacol 2019:10:9.

- [13] Wei HM, Wu HJ, Yu W, et al. Shenfu decoction as adjuvant therapy for improving quality of life and hepatic dysfunction in patients with symptomatic chronic heart failure. J Ethnopharmacol 2015; 169:347–55.
- [14] Wang YJ, He LQ, Sun W, et al. Optimized project of traditional Chinese medicine in treating chronic kidney disease stage 3: a multicenter double-blinded randomized controlled trial. J Ethnopharmacol 2012;139:757–64.
- [15] Zhang CT, Yang HJ, Gan WF, et al. A randomized controlled trial for prevention of acute exacerbation of stable chronic obstructive pulmonary disease with acupoint application of traditional Chinese medicine Study protocol clinical trial (SPIRIT Compliant). Medicine (Baltimore) 2020:99:8.
- [16] Wu QY, Yu XQ, Li JS. Literature analysis on the effect-related factors of acupoint application for chronic obstructive pulmonary disease (Chinese). J Tradit Chin Med 2012;53:331–4.
- [17] Liu H. Acupuncture combined with acupoint application improves symptoms, daily life quality and lung function in chronic obstructive pulmonary disease patients during acute exacerbation (Chinese). Acupunct Res 2016;41:251–4.
- [18] Li J, Hu GX, Cheng ZH, et al. Clinical observation of Chinese medicin eacupoin t sticking on prevention and treatment for recurrence of chronic obstructive pulmonary disease (Chinese). China J Tradit Chin Med Pharm 2013;028:1743–5.
- [19] Hu FZ, Sun HH, Wu ZL, et al. Effect of TCM acupoint application on immune function of patients with chronic obstructive pulmonary disease at stable period (Chinese). Modern J Integrated Tradit Chin Western Med 2017;26:2203–5.
- [20] Chronic Obstructive Pulmonary Disease Group CTSGuidelines for the diagnosis and treatment of chronic obstructive pulmonary disease (2013 revision) (Chinese). Chin J Tuberculosis Resp Dis 2013;36:255–64.
- [21] Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. BMJ 2009;339:3.
- [22] Vogelmeier CF, Criner GJ, Martinez FJ, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive lung disease 2017 report: GOLD executive summary. Eur Resp J 2017;49:32.
- [23] Cai S, Qin L, Tanoue L, et al. Effects of one-hour training course and spirometry on the ability of physicians to diagnose and treat chronic obstructive pulmonary disease. PLoS One 2015;10:10.
- [24] Chan SMH, Selemidis S, Bozinovski S, et al. Pathobiological mechanisms underlying metabolic syndrome (MetS) in chronic obstructive pulmonary disease (COPD): clinical significance and therapeutic strategies. Pharmacol Ther 2019;198:160–88.
- [25] McGarvey LP, John M, Anderson JA, et al. Ascertainment of causespecific mortality in COPD: operations of the TORCH Clinical Endpoint Committee. Thorax 2007;62:411–5.
- [26] Spilling CA, Bajaj MPK, Burrage DR, et al. Contributions of cardiovascular risk and smoking to chronic obstructive pulmonary disease (COPD)-related changes in brain structure and function. Int J Chronic Obstr Pulm Dis 2019;14:1855–66.
- [27] Tan WC, Mahayiddin AA, Charoenratanakul S, et al. Global initiative for chronic obstructive lung disease strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease: an Asia-Pacific perspective. Respirology 2005;10:9–17.
- [28] Celli BR, Thomas NE, Anderson JA, et al. Effect of pharmacotherapy on rate of decline of lung function in chronic obstructive pulmonary diseaseresults from the TORCH study. Am J Respir Crit Care Med 2008;178:332–8.
- [29] Stringer W, Marciniuk D. The role of cardiopulmonary exercise testing (CPET) in pulmonary rehabilitation (PR) of chronic obstructive pulmonary disease (COPD) patients. COPD-J Chronic Obstr Pulm Dis 2018;15:621–31.