Study Protocol

The use of mindfulness-based stress reduction (MBSR) for lung cancer patients: protocol for a systematic review and meta-analysis

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Background: Mindfulness-based stress reduction (MBSR) intervention has been extensively applied in cancer patients for relieving symptom burden and its effectiveness has also been demonstrated. However, the effectiveness of MBSR on psychological and physical functions in lung cancer patients has not yet been determined. The aim of the present systematic review and meta-analysis seeks to determine the role of MBSR in lung cancer patients.

Methods: A systematic search of PubMed, EMBASE, Cochrane Library, and China National Knowledgement Infrastructure (CNKI) will be carried out from their inception until to December 30, 2020. Studies investigating the comparative effects between MBSR and control groups on psychological and physical outcomes will be documented. Data concerning studies, patient characteristics, and outcomes will be extracted. Methodological quality of each eligible randomized controlled trial (RCT) will be assessed individually by two investigators independently using criteria recommended in the Cochrane Handbook for Systematic Reviews of Interventions 5.1.0. Meanwhile, Newcastle-Ottawa Quality Assessment Scale (NOS) will be used to assess methodological quality of non-randomized studies. All statistical analyses will be performed with RevMan and STATA softwares.

Discussion: The role of MBSR in lung cancer patients has not yet been demonstrated. This systematic review and meta-analysis will further determine the effectiveness of MBSR on psychological and physical outcomes and QoL among lung cancer patients, which will provide golden references for developing psychological interventions in order to improve patient care and designing future studies to bridge the gap between research findings and clinical practice.

Trial registration: We registered the protocol of this systematic review and meta-analysis in Open Science Framework (OSF) platform with a registration DOI of 10.17605/OSF.IO/MWVBQ (available from: https://osf.io/mwvbq).

Keywords: Lung cancer; psychological function; physical function; protocol; systematic review

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Introduction

Lung cancer is the second most common type of cancer worldwide and also the first-rank reason of causing cancer-related death (1). The increasing incidence of lung cancer can be attributed to numerous aspects, such as aging of population and environmental pollution (2). It is reported that the new cases of lung cancer have been more than 2.20 million, and approximately 1.80 million deaths in 2020 have been estimated (1).

Although a series of treatment modalities such as surgical operation, chemotherapy, radiotherapy, immuno-biological cancer therapy, and complementary and alternative therapy have been used for treating lung cancer (3-5), patients remain experiencing many serious symptoms such as fatigue (6) and symptom distress (7) because all treatments have also destructive effects on both cancer and normal cells (8). Moreover, cancer self also play a critical role in the development of symptoms (9,10). Previous studies revealed that lung cancer patients experienced more symptom burden than patients who were diagnosed with other types of cancer (7,9,11). It is acknowledged that these all symptoms are significantly associated with reduced psychosocial and physical functions among lung cancer patients (8,12). Additionally, the negative association between symptoms and quality of life (QoL) has also been established by several studies (13-15).

Previous findings have evidently established the effects of psychosocial interventions in improving psychological and physical wellbeing and QoL of cancer patients (16-18). As one of the most common psychosocial interventions, mindfulness-based stress reduction (MBSR) has been extensively applied in cancer patients (18,19). MBSR program was initially developed by Kabat-Zinn to consist of an 8-week psycho-educational program and four meditative techniques including sitting meditation, body scan, gentle Hatha yoga, and walking meditation (20-22). Training of MBSR will make participants gradually to be out of dysfunctional thoughts and directly perceive the emotions and bodily sensations at the present moment via repeatedly bring participants' attention back to the present moment (23). As a result, MBSR program enable participants to step back from ruminating about the past or worrying about the future and simply unfold experiences of the present moment (21). MBSR has been demonstrated to be effective in relieving symptom burden and improving psychosocial adjustment to disease and QoL to date (18,19,24,25). Some studies also tried to investigate the effects of MBSR in lung cancer patients (26,27) and other lung diseases such as interstitial lung diseases (28,29). However, the systematic review and meta-analysis specifically for lung cancer patients is greatly limited except for one meta-analysis which investigated the effects of MBSR on fatigue among lung cancer with subgroup analysis (24).

Therefore, we conduct the current systematic review and meta-analysis to comprehensively evaluate the benefits of MBSR on psychological and physical functions and QoL in patients with lung cancer. We present the following article in accordance with the PRISMA reporting checklist (available at http://dx.doi.org/10.21037/apm-21-194) (30).

Methods

We designed the methodological framework of this systematic review and meta-analysis protocol in accordance with the methodology recommended by the Cochrane handbook (31). Additionally, we will report our findings in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (32). No ethics approval and informed consent will be required because all statistical analysis will be performed based on published studies without involvement of patients. The protocol of this systematic review and meta-analysis has been registered in Open Science Framework (OSF) platform on 22 January, 2021. A registration DOI of 10.17605/OSF.IO/MWVBQ has been approved (available from: https://osf.io/mwvbq).

Search strategy

We will electronically search PubMed, EMBASE, Cochrane Library, and China National Knowledgement Infrastructure (CNKI) for potentially eligible studies from their inception to December 30, 2020. We will construct the search strategy with the combination of medical subject heading (MeSH) terms and text words. We will verify the systematic review and meta-analysis which also focused our topic and the bibliographies of eligible studies in order to add any additionally eligible study. As an example, we summarized the search strategy of PubMed in *Table 1*. The process of identification and selection of literature will be displayed in *Figure 1*. Any disagreement about retrieval of eligible studies will be settled through consulting a third senior author.

Study selection

One study will be included in the current systematic review

Table 1 Search strategy of PubMed

Search number	Query
7	#3 AND #6
6	#4 OR #5
5	((((((Pulmonary Neoplasms[Title/Abstract]) OR (Lung Neoplasm[Title/Abstract])) OR (Pulmonary Neoplasm[Title/Abstract])) OR (Lung Cancer[Title/Abstract])) OR (Lung Cancers[Title/Abstract])) OR (Pulmonary Cancer[Title/Abstract])) OR (Pulmonary Cancers[Title/Abstract])
4	"Lung Neoplasms"[Mesh]
3	#1 OR #2
2	((((mindfulness[Title/Abstract]) OR (mindfulness meditation[Title/Abstract])) OR (mindfulness-based stress reduction[Title/Abstract])) OR (mindfulness based stress reduction[Title/Abstract])) OR (MBSR[Title/Abstract])
1	"Mindfulness"[Mesh]

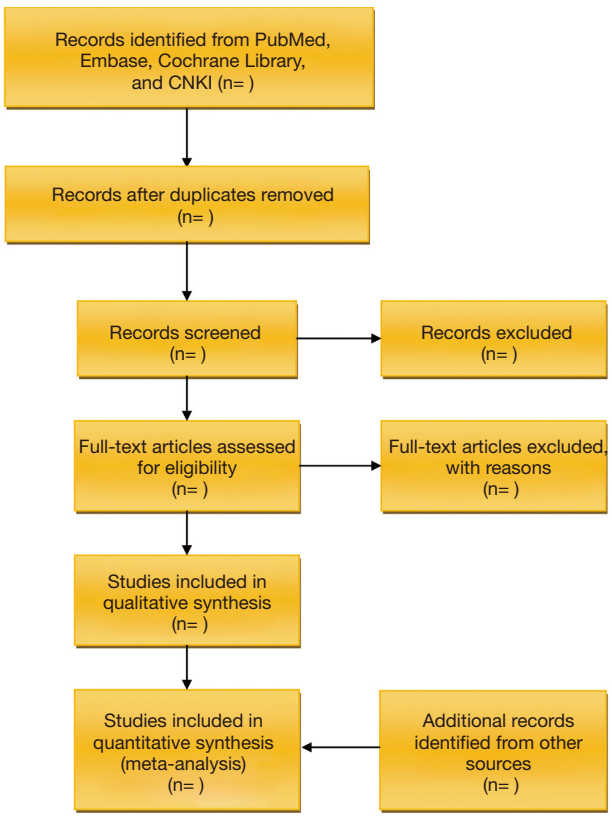

Figure 1 The process of identification and selection of literature.

and meta-analysis if the following criteria were covered: (I) patients, with the age of 18 years or older and irrespective of gender, were diagnosed with lung cancer; (II) MBSR in research group; (III) usual care (UC) or no intervention in control group; (IV) psychological and physical outcomes such as self-designed efficacy and cancer-related fatigue which were defined as primary outcomes and QOL which was defined as secondary outcome; (V) clinical controlled trial (CCT) and randomized clinical trial (RCT); (VI) only full text published in English and Chinese language will be eligible for our inclusion criteria.

One study will be excluded if it covered at least one of the following criteria: (I) MBSR was not used in research group; (II) included mixed patients; and (III) protocol, unpublished or duplicate without adequate information or poor quality.

Data extraction

Two authors will be assigned to independently extract essential data with designed information extraction form (*Table 2*). The following information will be extracted from eligible studies: basic information eligible study including author, publication year and country, basic information of patients including sample size, age and tumor staging such as TNM stage, basic information of regimes including details of interventions, outcomes and study design, and information of methodological quality. Quantitative data will be extracted to estimate effect sizes. Data on effect size that could not be obtained directly will be recalculated when possible. Qualitative information will also be summarized to systematically describe the effects and safety of MBSR. Any disagreement about data extraction will be resolved through consulting a third senior author.

Methodological quality assessment

Two authors will be assigned to independently assess the methodological quality of eligible studies. Methodological quality of individual RCT will be appraised with the

Table 2 Basic characteristics of all eligible studies

Study	Country	Sample size	Age, year	Interventions		Follow-up	Outcomes	Instruments	Study design
				RG	CG				
Study 1									
Study 2									
Study 3									
.....									

Cochrane risk of bias tool as following six domains including (33): (I) random sequence generation; (II) allocation concealment; (III) blinding of personnel, participants, and assessors; (IV) incomplete outcome data; (V) selective reporting; and (VI) other bias. Additionally, methodological quality of nonrandomized studies will be assessed with Newcastle-Ottawa Quality Assessment Scale (NOS) from three aspects: selection of study groups, comparability of study groups and ascertainment of either the exposure or outcome of interest (34). Any disagreement about the methodological quality assessment will be resolved through consulting a third senior author.

Statistical analysis

For continuous outcomes, we will calculate the differences between two groups as the standard mean difference (SMD) or mean difference (MD) with 95% confidence interval (CI). For categorical outcomes, we will use risk ratio (RR) with 95% CI to express pooled estimates. In this meta-analysis, we only extract immediate, post-intervention data (after a 6–16 week course) to estimate the effect size in order on achieve uniformity according to the methods used in previous meta-analysis (17). Meanwhile, we also extract the data at the first time point which is defined as immediately post-intervention for statistical analysis if a study reported data on a series of time points. Before performing statistical analysis, we will use Cochrane's Q test and the I^2 statistic to qualitatively and quantitatively evaluate the heterogeneity across studies accordingly (35,36). Nevertheless, we will only perform a random-effects model to calculate all pooled results regardless of actual level of heterogeneity across studies because substantial variations in population, interventions, and outcome measures are inevitable. A $P<0.05$ will be considered to be the criteria of statistical significance. All statistical analyses will be conducted using Review Manager (RevMan) version 5.3 (Cochrane Collaboration, Oxford, United Kingdom).

Publication bias

For individual outcome, we will draw funnel plot and perform Egger's tests respectively to test the possibility of publication bias when accumulated number of 10 were achieved (37-39). STATA 14.0 software (StataCorp, Texas, USA) will be utilized to complete Egger's tests.

Quality of evidence assessment

We will use the Grading of Recommendations Assessment, Development and Evaluation method (40) to grade the overall quality of evidence of quantitative pooled results as high, moderate, low, or very low after completing all statistical analyses. With the GRADE system, the level of RCT will be initially rated as high, and the level can be downgraded according to five aspects including risk of bias, inconsistency, indirectness, imprecision, and publication bias. Two authors will independently rate the level of evidence and any disagreement will be resolved based on the consensus principle.

Discussion

As one of the most common malignant tumors around the world, lung cancer was estimated to account for 11.4% new cancer cases and 18.0% cancer deaths in 2020 (41). Evidence suggested lung cancer patients will experience a series of serious symptoms due to the negative impact of definitive diagnosis of cancer and anticancer treatments (7,9). As a result, lung cancer patients will also suffer from poor psychological and physical functions and QoL (6,7). As one of the most common psychological intervention programs, MBSR have been extensively investigated and also established to improve symptoms of cancer patients

(19,24,26). However, there was no systematic review and meta-analysis specifically focused on the impacts of MBSR intervention on psychological and physical functions and QoL of lung cancer patients has been reported to date. As a result, it remains unclear whether MBSR should be preferentially prescribed for the treatment of psychological and physical conditions among lung cancer patients. The present systematic review and meta-analysis will provide a comprehensive summary of studies exploring the effectiveness of MBSR on psychological and physical outcomes and QoL in lung cancer patients.

To our knowledge, this is the first systematic review and meta-analysis of RCTs and CCTs that will investigate the effects of MBSR on psychological and physical outcomes and QoL for lung cancer patients. However, we also must further interpret the limitations in this systematic review and meta-analysis. First, we will only search four databases including PubMed, EMBASE, Cochrane Library and CNKI, and thus some potentially eligible studies included in other databases such as Web of Science and SCOPUS may be missed. Second, the substantial variations in intensity, frequency, and duration of MBSR across studies may introduce heterogeneity, we thus use a random-effects model to perform all statistical analyses, which will result in wider 95% CI. Third, definitions of usual care in individual study are different, however subgroup analysis will not be designed because details of usual care were not introduced.

Conclusions

The systematic review and meta-analysis will investigate the effectiveness of MBSR intervention on psychological and physical functions and QoL in patients with lung cancer. The results from the current study will demonstrate the effects of MBSR on specific outcomes and then provide evidence for developing psychological interventions in clinical practice. Meanwhile, this study also determines the gap between research findings and clinical practice, and then provides references for designing further studies.

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Footnote

Reporting Checklist: The authors have completed the PRISMA reporting checklist. Available at http://dx.doi.org/10.21037/apm-21-194

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/apm-21-194). Dr. XT reports grants from the Technological Innovation and Demonstrational Application Project of Chongqing Science and Technology Bureau (project No. cstc2018jscx-msybX0030) and Chongqing Natural Science Foundation (project No. cstc2018jcyjAX0737s). The other authors have No conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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