The efficacy of mindfulness-based intervention for heart diseases
A meta-analysis of randomized controlled trials
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Abstract
Introduction: The efficacy of mindfulness-based intervention for heart diseases remains controversial. We conduct a systematic review and meta-analysis to explore the impact of mindfulness-based intervention on heart diseases.

Methods: We have searched PubMed, EMBase, Web of science, EBSCO, and Cochrane library databases through August 2020 for randomized controlled trials (RCTs) assessing the effect of mindfulness-based intervention versus usual care on heart diseases. This meta-analysis is performed using the random-effect model.

Results: Five RCTs involving 458 patients are included in the meta-analysis. Overall, compared with control group for heart diseases, mindfulness-based intervention is associated with significantly increased 6 minute walking test [mean difference (MD) = 14.74; 95% confidence interval (95% CI) = 2.50–26.97; \(P = .02\)], decreased heart rate (MD = −2.54; 95% CI = −4.76 to −0.31; \(P = .03\)) and stress score (MD = −2.31; 95% CI = −4.23 to −0.38; \(P = .02\)), but shows no obvious impact on anxiety score (MD = −3.48; 95% CI = −7.98 to 1.03; \(P = .13\)) or respiratory rate (MD = −0.42; 95% CI = −1.31 to 0.46; \(P = .35\)).

Conclusions: Mindfulness-based intervention can provide additional benefits to heart diseases.

Abbreviations: 6MWT = 6 minute walking test, CI = confidence interval, MD = mean difference, RCTs = randomized controlled trials.

Keywords: heart diseases, meta-analysis, mindfulness-based intervention, randomized controlled trials.

1. Introduction
Heart diseases has become the foremost cause of health burden worldwide.[1–4] These diseases can result in significant stress, chronic stressors such as anxiety and depression which are regarded as the independent risk factors for cardiovascular.[5–7] Chronic stress can not only reduce the quality of life, but also negatively affect some physiological parameters such as respiration rate, heart rate, blood pressure, inflammatory markers and brain activity.[8–10]

Thus, methods targeting stress reduction may have a beneficial effect for the prognosis of heart diseases with the respect to heart rate and physical fitness. Lifestyle interventions such as mindfulness therapy obtains the increasing attention.[11,12] Mindfulness is defined as the capacity to live with open and non-judgmental awareness towards all experiences within the present moment.[13] Mindfulness therapy has showed the potential in improving the psychological outcomes in patients with chronic pain, obesity, hypertension, depression, anxiety and cardiovascular disease.[14–16]

The efficacy of mindfulness-based intervention for heart diseases has not been well established. Recently, several studies on the topic have been published, and the results have been conflicting.[13,17,18] With accumulating evidence, we therefore perform a systematic review and meta-analysis of RCTs to investigate the efficacy of mindfulness-based intervention versus usual care for heart diseases.

2. Materials and Methods
Ethical approval and patient consent are not required because this is a systematic review and meta-analysis of previously published studies. The systematic review and meta-analysis are conducted and reported in adherence to Preferred Reporting Items for Systematic Reviews and Meta-Analyses.[19]

2.1. Search strategy and study selection
Two investigators have independently searched the following databases (inception to August 2020): PubMed, EMBase, Web of science, EBSCO, and Cochrane library databases. The electronic search strategy is conducted using the following
keywords: “mindfulness” and “heart diseases.” We also check the reference lists of the screened full-text studies to identify other potentially eligible trials.

The inclusive selection criteria are as follows: patients are diagnosed with heart diseases; intervention treatments are mindfulness-based intervention versus control intervention; and study design is RCT.

2.2. Data extraction and outcome measures

We have extracted the following information: author, number of patients, age, gender, systolic blood pressure, detail methods in each group, etc. Data have been extracted independently by 2 investigators, and discrepancies are resolved by consensus. We also contact the corresponding author to obtain the data when necessary.

The primary outcomes are 6 minute walking test (6MWT) and heart rate. Secondary outcomes include stress score, anxiety score, and respiratory rate.

2.3. Quality assessment in individual studies

Methodological quality of the included studies is independently evaluated using the modified Jadad scale.[20] There are 3 items for Jadad scale: randomization (0–2 points), blinding (0–2 points), dropouts and withdrawals (0–1 points). The score of Jadad Scale varies from 0 to 5 points. An article with Jadad score ≤ 2 is considered to be of low quality. If the Jadad score ≥ 3, the study is thought to be of high quality.[21]

2.4. Statistical analysis

We estimate the mean difference (MD) with 95% confidence interval (CI) for all continuous outcomes. A random-effects model is used regardless of heterogeneity. Heterogeneity is reported using the $I^2$ statistic, and $I^2 > 50\%$ indicates significant heterogeneity.[22] Whenever significant heterogeneity is present, we search for potential sources of heterogeneity via omitting 1 study in turn for the meta-analysis or performing subgroup analysis. All statistical analyses are performed using Review
3. Results

3.1. Literature search, study characteristics, and quality assessment

A detailed flowchart of the search and selection results is shown in Figure 1. One hundred eighty five potentially relevant articles are identified initially. Finally, 5 RCTs that meet our inclusion criteria are included in the meta-analysis.\(^{[13,17,18,23,24]}\)

The baseline characteristics of the 5 eligible RCTs in the meta-analysis are summarized in Table 1. The 5 studies are published between 2003 and 2018, and sample sizes range from 18 to 324 with a total of 458. The duration of mindfulness-based intervention varies from 6 to 12 weeks.

Among the 5 studies included here, 2 studies report 6MWT and heart rate,\(^{[13,17]}\) 2 studies report stress score,\(^{[13,23]}\) 3 studies report anxiety score,\(^{[13,23,24]}\) and 2 studies report respiratory rate.\(^{[13,17]}\) Jadad scores of the 5 included studies vary from 3 to 4, and all 5 studies are considered to be high-quality ones according to quality assessment.

3.2. Primary outcomes: 6MWT and heart rate

These outcome data were analyzed with the random-effects model, and the pooled estimate of the 2 included RCTs suggested that compared to control group for heart diseases, mindfulness-based intervention is associated with significantly increased 6MWT (MD = 14.74; 95% CI = 2.50–26.97; \(P = .02\)), with no heterogeneity among the studies (\(I^2 = 0\%, \text{ heterogeneity } P = .67\)) (Fig. 2) and decreased heart rate (MD = −2.54; 95% CI = −4.76 to −0.31; \(P = .03\)), with no heterogeneity among the studies (\(I^2 = 0\%, \text{ heterogeneity } P = .03\)) (Fig. 3).

3.3. Sensitivity analysis

No heterogeneity is observed among the included studies for the primary outcomes, and thus we do not perform sensitivity analysis via omitting 1 study in turn to detect the heterogeneity.

3.4. Secondary outcomes

Compared to control group for heart diseases, mindfulness-based intervention can significantly reduce stress score (MD = −2.31; 95% CI = −4.23 to −0.38; \(P = .02\); Fig. 4), but reveals no obvious influence on anxiety score (MD = −3.48; 95% CI = −7.98 to 1.03; \(P = .13\); Fig. 5) or respiratory rate (MD = −0.42; 95% CI = −1.31 to 0.46; \(P = .35\); Fig. 6).

3.5. Publication bias

No publication bias was observed (\(P > .05\)) based on Begg test and Egger regression test.

4. Discussion

Limited exercise capacity is an important predictor for outcome for cardiac disease, and is associated with survival.\(^{[25–28]}\) The decrease in physical performance indicates the adverse outcomes in patients with congenital heart disease. Cardiac rehabilitation programs were revealed to reduce the total and cardiovascular mortality in patients with post-myocardial infarction.\(^{[29,30]}\) Our results of this meta-analysis indicated that mindfulness-based intervention could be part of future treatment modalities to improve physical performance in heart disease patients as evidenced by the increase in 6MWT.
In addition, heart rate is known as another important index to predict long-term survival, and the reduction in heart rate is recommended in the management and prevention of heart diseases. In patients with hypertension, acute coronary syndromes, stable coronary heart disease and heart failure, heart rate is proved to be a risk factor for cardiovascular and all-cause mortality. The heart rate is also substantially decreased by mindfulness-based intervention in patients with heart diseases based on the results of our meta-analysis.

Furthermore, a pilot study reported that mindfulness-based intervention program resulted in significant reduction in depression and perceived stress in patients with coronary artery disease. The reduction in stress after treatment with mindfulness-based intervention was also confirmed in this meta-analysis. Mindfulness-based stress-reduction was also documented to improve anxiety, emotional control and coping than resting-stress hormones or physical functioning. Although there is no heterogeneity in this meta-analysis, different methods and duration of mindfulness-based intervention, and various levels of severity may also produce some bias.

This meta-analysis has several potential limitations. Firstly, our analysis is based on only 5 RCTs, and 4 of them have a relatively small sample size (n < 100). Overestimation of the treatment effect was more likely in smaller trials compared with larger samples. Next, although there is no heterogeneity, different methods and duration of mindfulness-based intervention,
as well as various levels of severity may result in some bias. Finally, some unpublished and missing data may lead to some bias for the pooled effect.

5. Conclusions
Mindfulness-based intervention is effective to improve the outcomes of heart diseases.

Author contributions
Qingxia Kang conducted the design, study planning, data analysis and data interpretation. Aihua Luo wrote and revised the article. All authors read and approved the final manuscript.

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