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## Review Article

## Meta-analysis of meditative/relaxation-based interventions for cognitive impairment in cancer patient

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## ABSTRACT

**Objective:** This meta-analysis aimed to review any form of meditative/relaxation interventions for managing cognitive impairment in cancer patients, and to examine its intervention effect.**Methods:** Three databases (PubMed, PsycInfo, and CNKI) were searched until September 30, 2016. Randomized controlled trials (RCTs) of meditative/relaxation-based interventions for the management of cognitive impairment in cancer patients were considered for inclusion.**Results:** A total of 4 RCTs were included in this meta-analysis. Four RCTs with a total of 290 subjects indicated that meditative/relaxation interventions significantly improved subjective cognitive function of cancer patients. The weighted mean difference was 5.29 (95% CI: 2.97, 7.61). The overall effect of Z score was 4.47 ( $P < 0.001$ ). The meditative/relaxation-based interventions had positive effects on the physical and mental QOL (quality of life) of cancer patients. Although the improvement of physical QOL was in favor of interventions, there is no statistically significant difference (Z score = 1.81,  $P = 0.07$ ). For the effects of meditative/relaxation interventions on mental QOL, there is significantly statistical difference (Z score = 2.99,  $P = 0.003$ ). All included RCTs had a follow-up assessment within six months.**Conclusion:** Meditation-based interventions had statistically significant difference in improve subjective cognitive function and mental QOL in cancer patients. However, since the conclusion of this meta-analysis was drawn based on limited number of RCTs, future research should be conducted to confirm its positive intervention effects.© 2017 Chinese Nursing Association. Production and hosting by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

## 1. Introduction

The prevalence of cognitive impairment in cancer patients is up to 75% [1]. While cancer and its treatment-induced cognitive impairment is usually mild to moderate [2], it exerts a substantial impact on a survivor's ability to perform daily task and impact their long-term quality of life (QOL) [2,3].

As pharmacological interventions used to improve cognitive function and reduce cognitive impairment have significant treatment side-effects [4], meditative/relaxation-based interventions are emerged to be applied for reducing cognitive impairment in cancer patients. Meditative/relaxation-based intervention is

defined as a mental-dominated exercise that involves reaching a focused state of mind and may include breathing and relaxation exercises, including meditation, exercise of yoga, Taichi or Qigong [5]. The mechanism of meditative/relaxation-based interventions for improve cognitive impairment may through stress reduction, so that it may directly or indirectly help the immune system for regulating the cytokine production [3,5].

## 2. Methods

## 2.1. Study types

Three databases of PubMed, PsycInfo, and CNKI were searched till September 30, 2016, including articles published in both English and Chinese. Studies were eligible for inclusion if they were randomized controlled trials (RCTs), which addressed the effects of meditative/relaxation-based interventions on reducing cognitive

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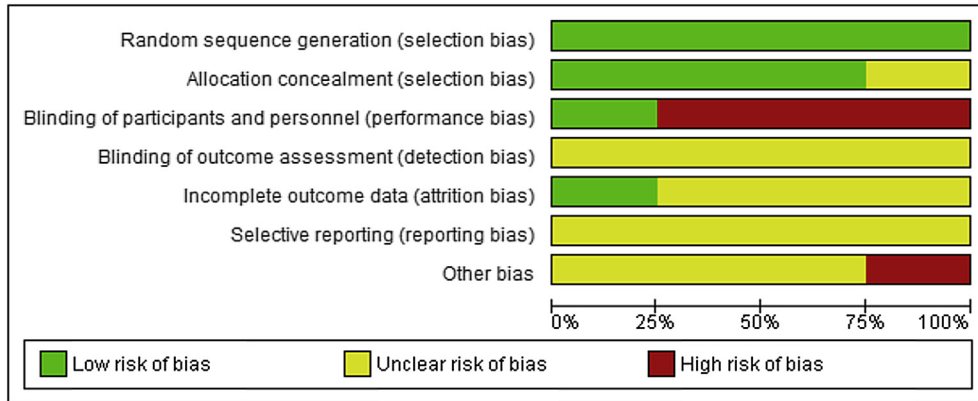


Fig. 1. Summary of risk of bias of included RCTs.

impairment of adult patients with cancer. RCTs included brain or central nervous system tumors were excluded due to these types of tumor can directly impact the cognitive function of cancer patients.

2.2. Study participants

Patients diagnosed with primary cancer during adulthood-onset (aged 18 years or older), because patient-reported cognitive function measures for childhood-cancer survivors differ from adult measures, and are not diagnosed with a non-brain or non-central nervous system (CNS) tumor, as a brain or CNS tumor can directly impact the brain, and thus the cognitive processes, of cancer survivors.

2.3. Types of interventions and outcome measures

This meta-analysis included any form of meditative/relaxation-based interventions such as meditation, exercise of yoga, Taichi or Qigong. The primary outcome was cognitive function by subjective and/or objective cognition outcome measures. The secondary outcome was quality of life as a result of meditative/relaxation-based interventions.

2.4. Data extraction and assessment of bias risk

For each included RCT, data was independently extracted by two researchers, and disagreement on data extraction was resolved by discussion and verified by the third researcher. The Cochrane Collaboration’s Review Manager (RevMan 5.3) [6] was used to evaluate the risk of bias of the included RCTs. The Cochrane Risk of Bias Assessment Tool consists of seven domains including “random sequence generation, allocation concealment, blinding of participants and research personnel, blinding outcome assessment, incomplete outcome data, selective outcome reporting and other

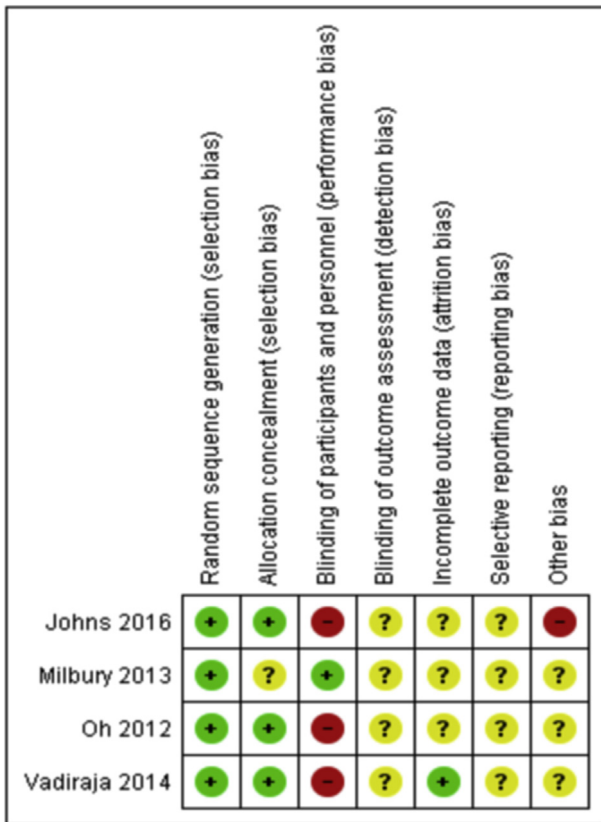


Fig. 2. Risk of bias for each included RCT.

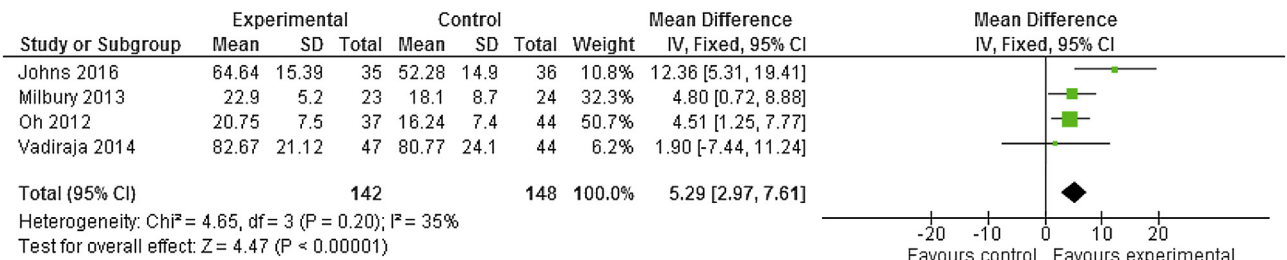


Fig. 3. Effects of meditative/relaxation-based interventions on subjective cognitive function.

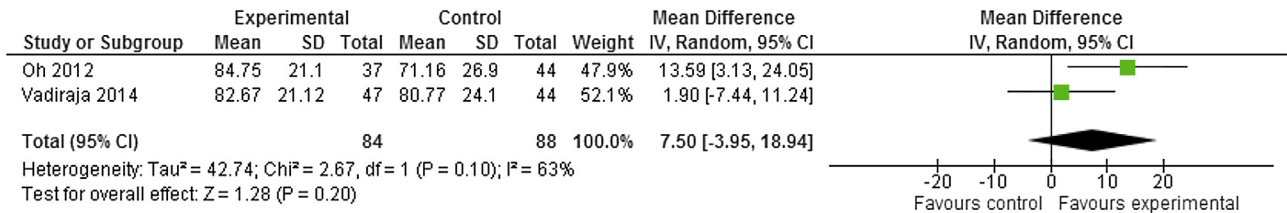


Fig. 4. Effects of Qigong or Yoga interventions on subjective cognitive function.

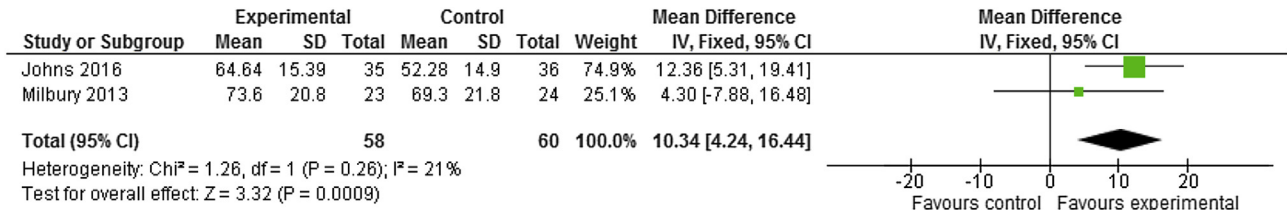


Fig. 5. Effects of medication interventions on subjective cognitive function.

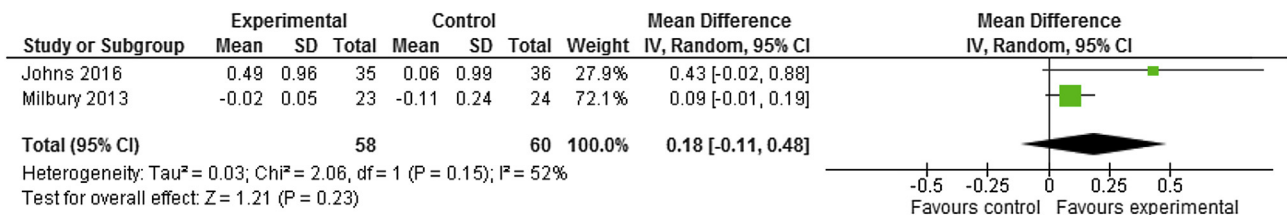


Fig. 6. Effects of meditation intervention on objective cognitive function in cancer patients.

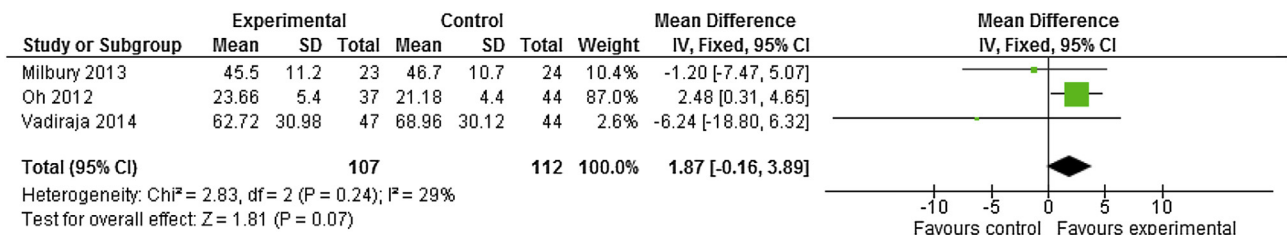


Fig. 7. Effects of meditative/relaxation-based interventions on physical QOL.

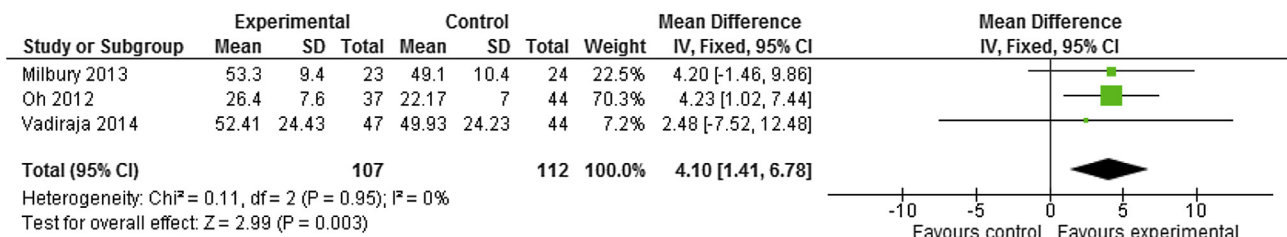
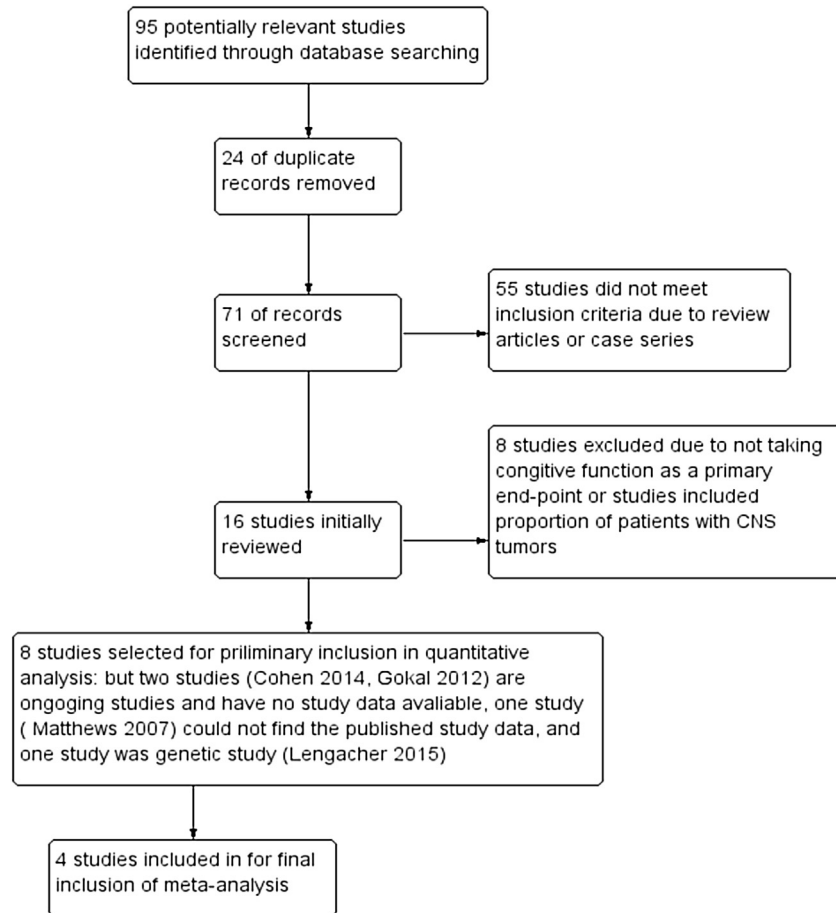


Fig. 8. Effects of meditative/relaxation-based interventions on mental QOL.



Graph 1. Study searching diagram.

biases” [7]. Fig. 1 shows the results of Risk of Bias for those included RCTs in this meta-analysis.

### 2.5. Data synthesis and analysis

Data pooling of this meta-analysis was performed for the effects of meditation/relaxation interventions on the subjective and objective cognitive function outcome measures by using the Cochrane statistical software, RevMan 5.3 [6]. The heterogeneity of included RCTs was assessed using  $I^2$  statistics, an  $I^2$  value of more than 50% was considered to be indicative of statistical heterogeneity, the value of less than 50% was taken as homogeneity [7]. Accordingly, the random-effect model was used to combine statistically heterogeneous RCTs, and the fixed-effect model was applied to combine statistically homogeneous RCTs [7].

### 3. Results

Results of study searching diagram was shown in Graph 1. There were a total of 16 articles initially included, but eight studies were not eligible so that they were excluded from this meta-analysis. Of these 8 trials, two of them were ongoing trials and had no data available yet. Another completed trial had no published data available, and the fourth excluded trial was generic study for exploring the mechanism of meditative intervention effects.

Each trial was assessed its risk of bias which was shown in Fig. 2. The highest risk of bias was “blinding the participants and personnel”. Of the 4 RCTs, two of them used the meditation

intervention programs [5,8], two other RCTs used the intervention of Qigong [9] and Yoga [10], respectively.

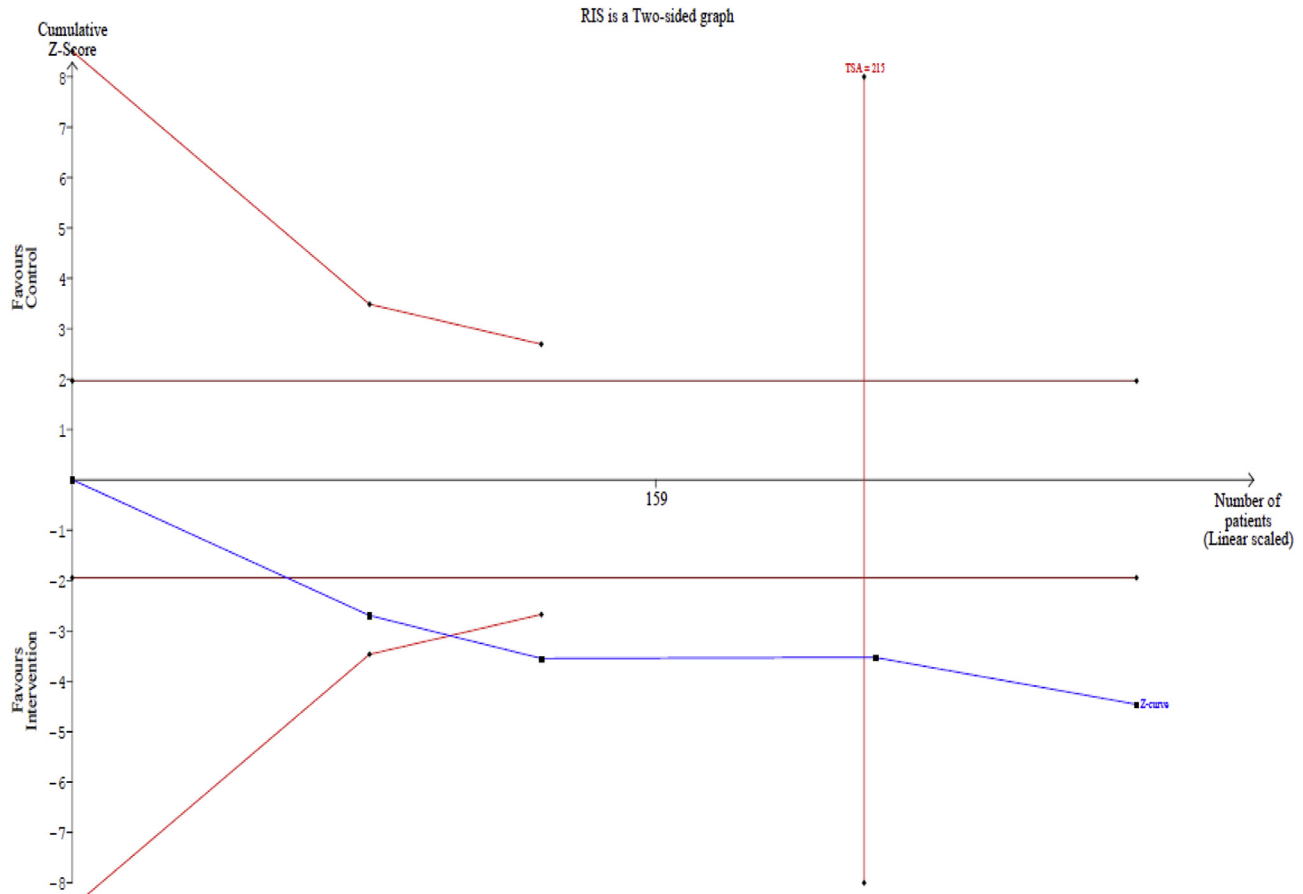
The intervention duration ranged from 6 weeks to 10 weeks, the frequency of interventions was mainly one session per week. Subjective cognitive measures include FACT-Cog (Functional Assessment of Cancer Therapy-Cognitive Function), EORTC-CF (European Organization for Research and Treatment of Cancer-Cognitive Function), and AFI (Attentional Function Index). Objective measures include RAVLT (Rey Auditory Verbal Learning Test), Digit Symbol, and Stroop test. QOL measures include SF-36 and EORTC QLQ-C30.

For the effects of interventions on subjective cognitive function in cancer patients, four RCTs with a total of 290 subjects indicated that meditative/relaxation interventions significantly improved subjective cognitive function of cancer patients. Fig. 3 shows the weighted mean difference (WMD) was 5.29 (95% CI: 2.97, 7.61). The overall effect of Z score was 4.47 ( $P < 0.00001$ ).

By using Trial Sequential Analysis (TSA, developed by The Copenhagen Trial Unit, Center for Clinical Intervention Research, Denmark, Available from [www.ctu.dk/tsa](http://www.ctu.dk/tsa)), we calculated the required information size (RIS) was 215 (Graph 2), and the total sample size of these four included trials was 290, as shown in Fig. 3.

By subgroup analysis, the effects of Qigong or Yoga also shows that the improvement of subjective cognitive function was in favor of intervention, but there is no statistically significant difference (Z score = 1.28,  $P = 0.20$ ) (Fig. 4).

In terms of subgroup analysis of meditation interventions for subjective cognitive function, Fig. 5 shows the WMD for the overall



Graph 2. Trial sequential analysis.

effect of meditation interventions was 10.34 (95% CI: 4.24, 16.44), and the overall effects has statistical significance (Z score = 3.32,  $P = 0.0009$ ).

For the meditative/relaxation-based interventions on objective cognitive function, only two RCTs [5,8] applied objective cognitive tests to examine its intervention effects. Fig. 6 indicates that the improvement of objective cognitive function was in favor of medication interventions, but there is no statistically significant difference (Z score = 1.21,  $P = 0.23$ ).

From Figs. 7 and 8, the meditative/relaxation-based interventions had positive effects on the physical and mental QOL of cancer patients. Although the improvement of subjective cognitive function was in favor of CR interventions, there is no statistically significant difference (Z score = 1.81,  $P = 0.07$ ) (Fig. 7). For the effects of interventions on mental QOL, there is significantly statistical difference (Z score = 2.99,  $P = 0.003$ ) (Fig. 8).

#### 4. Discussion

This meta-analysis found that the improvement of subjective and objective cognitive function was in favor of meditative/relaxation-based interventions, especially in the outcomes of subjective cognitive function. From Fig. 6, the effect of meditation interventions in the improvement of objective cognitive function could not be considered statistically significant due to the 95% CI of overall effect size crossed 0. As the causes of cognitive impairment in cancer patients are still unclear, quality research is required in order to determine the exact mechanism and cause of cognitive

impairment [11], which will help nurses and other healthcare providers to develop more effective intervention programs for reducing cognitive impairment in cancer patients.

While previous meta-analysis found that relaxation-based intervention of Yoga had statistically significant differences in enhancing QOL of breast cancer patients [12], this study only found that the effect of Yoga and meditation interventions on mental QOL had significantly statistical differences. From Fig. 6, as the 95% CI of weighted mean difference crossed 0, the effect of Yoga and meditation interventions on physical QOL means no statistical significance.

Although these included RCTs had low levels of risk of bias, all these trials only assessed the immediate effects at post-intervention or within an half year's follow-up, as longer-term follow-up assessment can monitor the sustainability of intervention effects. Thus, future research should be conducted in a longer-term follow-up to establish whether meditative/relaxation-based interventions have long-term effects on the improvement of cognitive function in cancer patients.

In addition, as the causes of cognitive impairment in cancer survivors are still unclear [11], it is difficult to determine which intervention strategies will be better than others although meditative/relaxation-based interventions show positive effects for improving cognitive function in cancer patients. Therefore, future research is required in order to determine the mechanism or causes of cognitive impairment in cancer patients, which will allow nurses and healthcare providers to design better intervention strategies to ameliorate this distress symptom for cancer patients [11].

## 5. Conclusion

In recent years, there is an increasing use of meditation/relaxation-based interventions for managing cognitive impairment in cancer patients. Mediation-based interventions had statistically significant difference in improve subjective cognitive function and mental QOL in cancer patients. However, since the conclusion of this meta-analysis was drawn based on limited number of RCTs, future research should be conducted to confirm its positive intervention effects.

## Appendix A. Supplementary data

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.ijnss.2017.03.010>.

## References

- [1] Wefel JS, Kesler SR, Noll KR, Schagen SB. Clinical characteristics, pathophysiology, and management of noncentral nervous system cancer-related cognitive impairment in adults. *CA Cancer J Clin* 2015;65:123–38.
- [2] Treanor CJ, McMenamin UC, O'Neill RF, Cardwell CR, Clarke MJ, Cantwell M, et al. Non-pharmacological interventions for cognitive impairment due to systemic cancer treatment. *Cochrane Database Syst Rev* 2016;8:CD011325. <http://dx.doi.org/10.1002/14651858.CD011325.pub2>.
- [3] Ganz PA. Doctor, will the treatment you are recommending cause chemobrain? *J Clin Oncol* 2012;30:229–31.
- [4] Gehring K, Roukema JA, Sitskoorn MM. Review of recent studies on interventions for cognitive deficits in patients with cancer. *Expert Rev Anticancer Ther* 2012;12:255–69.
- [5] Milbury K, Chaoul A, Biegler K, Wangyal T, Spelman A, Meyers CA, et al. Tibetan sound meditation for cognitive dysfunction: results of a randomized controlled pilot trial. *Psycho-Oncology* 2013;22(10):2354–63.
- [6] Higgins JPT, Green S, editors. *Cochrane handbook for systematic reviews of interventions*. The Cochrane Collaboration; 2011.
- [7] Review Manager (RevMan). 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014.
- [8] Johns SA, Von Ah D, Brown LF, Beck-Coon K, Talib TL, Alyea JM, et al. Randomized controlled pilot trial of mindfulness-based stress reduction for breast and colorectal cancer survivors: effects on cancer-related cognitive impairment. *J Cancer Surviv* 2016;10(3):437–48.
- [9] Oh B, Butow PN, Mullan BA, Clarke SJ, Beale PJ, Pavlakis N, et al. Effect of medical Qigong on cognitive function, quality of life, and a biomarker of inflammation in cancer patients: a randomized controlled trial. *Support Care Cancer* 2012;20(6):1235–42.
- [10] Vadiraja HS, Rao MR, Nagarathna R, Nagendra HR, Rekha M, Vanitha N, et al. Effects of yoga program on quality of life and affect in early breast cancer patients undergoing adjuvant radiotherapy: a randomized controlled trial. *Complement Ther Med* 2009;17(5–6):274–80.
- [11] Zeng YC, Cheng ASK, Chan CCH. Meta-analysis of the effects of neuropsychological interventions on cognitive function in non-central nervous system cancer survivors. *Integr Cancer Ther* 2016:1–11. <http://dx.doi.org/10.1177/1534735416638737>.
- [12] Zeng YC, Huang M, Cheng ASK, Zhou Y, So WKW. Meta-analysis of the effects of exercise intervention on quality of life in breast cancer survivors. *Breast Cancer* 2014;21(3):262–74. 2014.