

Dear Editor Prof Fang-Fang Ji, and Reviewer 2 and 3

Nov 27, 2016

We are grateful to the Editor, and Reviewer 2 and 3 for their insightful comments and useful suggestions, which have helped us improve our paper considerably. As indicated in the responses that follow, we have taken all the comments and suggestions into account in the revised version of the paper.

Editor

In accordance with the suggestion, we had asked the biomedical statistician to review the method in this study and to help interpretation of the data. In this revision, we added the unstandardized coefficients (B) and 95% CI for B in table 4 (table 3 in previous version) and probability for normality of each distribution in figure 1.

Reviewer 2

1. The study design is a cross-sectional study not an observational study
 - A. Thank you very much for pointing out our fundamental mistake about the study design. We have changed the study design to a **cross sectional study**.

2. The objective of the study should be changed to "to evaluate the correlation not the interaction"
 - A. In accordance with the reviewer's suggestion, we have changed the term from "interaction" to "**correlation**".

3. In methods part, the authors must give details regarding how to standardize radiographic evaluation including reliability test for KL classification.
 - A. In accordance with the reviewer's suggestion, we have amended the following sentences.

Subjects underwent a radiographic examination of both knees by posterior-anterior view in the fixed standing position by radiological technician. To avoid assessment error, all radiographs were assessed by two orthopedic physicians together. As the reviewer suggested, preferably radiographic assessment should be independently conducted for each

research.

4. In result part, table should include data regarding all relevant patient characteristics that might associated with outcomes eg underlying disease, educational level, previous treatment, etc.

A. Patient characteristics including underlying disease, educational level, and previous treatment are important factors for clinical outcome. However, the subjects in this study mostly consisted of elderly people (Fig.1), they usually have medication for age-related chronic diseases such as hypertension, hyperlipidemia and diabetes. As these complicated background factors might affect the results, we did not adopt these background parameters. In response to this comment, we have added the following sentences as a limitation of our study in the discussion section: **“Furthermore, we didn’t evaluate the patient’s background such as underlying disease, educational level and previous treatment which might be associated with clinical outcome.”**

However, as suggested by Reviewer 2, anxiety and depression are known to be deeply associated with catastrophizing. Therefore we re-interviewed subjects or rechecked their existing medical history, in terms of whether they took anti-anxiety drugs or anti-depressants at that time. We confirmed that no patient took these drugs, except for hypnotics, in this study.

5. Reference should be rechecked for both format and validity such as ref 16.

A. I have reconfirmed the references, and have made amendments where appropriate.

6. In discussion part, the author must spell out the important clinical implication of this study.

A. In accordance with the reviewer’s suggestion, we have added the clinical implication (in red) at the end of the discussion section.

“Taken together, this study suggests that clinicians should make sure to include an assessment of radiographic severity bilaterally and pain catastrophizing to explain the outcome measures in female patients with knee OA. **This is because they may be able to improve both functional capacity and symptoms even at a progressive stage without knee arthroplasty by psychological intervention, which ameliorates mal-adaptive**

cognition in patients with high catastrophizing thought.”

Reviewer 3

1. The K-L grading of the subject is the sum of that in right and left knee. The authors should refer previous papers on the sum of K-L grades when the patient has bilateral knee OA. Numbers of the patients with unilateral OA and bilateral OA should be indicated.

A. In accordance with the reviewer’s suggestion, we have counted the numbers of patients with unilateral OA and bilateral OA where OA was defined at least KL-2 on radiographic assessment. As a result, we have added the following sentences to Method & Table 2 in the Results section.

(Method)

Previous studies related to knee OA have assessed either side, although OA often affects bilateral knees (Felson et al. 1995) and this bilateralism may amplify the magnitude of symptoms (White et al. 2010). Firstly we assigned the subjects either into a unilateral group or a bilateral group according to whether radiographic knee OA was observed in one side or both sides.

(Results)

The subjects were assigned as follows: 17 subjects (22%) in the unilateral group and 60 subjects (78%) in the bilateral group. Comparisons of the dichotomous groups revealed that there were no significant differences in severity of knee pain and JKOM scores between the unilateral group and the bilateral group, while TUG was significantly faster in the unilateral group than in the bilateral group (Table 2).

2. Pain catastrophizing score is well associated with depression or anxiety. Does any patient have previous or current history of taking anti-anxiety drugs or antidepressant?

A. As suggested by the Reviewer, anxiety and depression are well known to be associated with pain catastrophizing. Therefore we re-interviewed the subjects again or rechecked their existing medical history to see whether they took anti-anxiety drugs or anti-depressants at that time. We confirmed that no patient took these drugs, except for hypnotics, in this study. We added the following sentences to the end of “Pain catastrophizing” in the

Method section.

Although catastrophizing is known to be a cognitive distortion closely linked to anxiety and depression (Sullivan et al. 1995), we confirmed that no subjects took anti-anxiety drugs or anti-depressants in the present study.

We hope you find our revised manuscript suitable for publication and look forward to hearing from you.

Sincerely,

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