Author’s response to reviews

Title: The Relationship between Pain Management and Psychospiritual Distress in Patients with Advanced Cancer Following Admission to a Palliative Care Unit

Authors:

Jaw-Shiun Tsai (jawshiun@ntu.edu.tw)
Ya-Ping Lee (b91401032@ntu.edu.tw)
Chih-Hsun Wu (wuyehsun@gmail.com)
Tai-Yuan Chiu (tychiu@ntuh.gov.tw)
Ching-Yu Chen (chency@nhri.org.tw)
Tatsuya Morita (tmorita@sis.seirei.or.jp)
Shou-Hung Hung (chaomei@ms14.hinet.net)
Sin-Bao Huang (heartbao@gmail.com)
Chia-Sheng Kuo (omigodokuo@gmail.com)

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Author’s response to reviews:

We thank the reviewers for the constructive and positive comments/suggestions. We have reanalyzed the data and revised the manuscript point by point accordingly.

Reviewer #1:

1. I had difficulty in understanding how in 7 days psychological & spiritual distress could be reduced to comfort level in the presence of severe pain from the study. No mention is made of further follow-up after 7 days.

Reply & Revision:

(1) Our palliative care team is multidisciplinary, providing physical, psychosocial and spiritual care simultaneously. It is a routine for us to adopt pharmacological and non-pharmacological strategies to relieve patients’ symptoms and psychological & spiritual distress.

(2) Based on our published studies, in general, our total care relieves not only physical symptoms but also psychological & spiritual distress, and is most effective one week
after admission. (ref: Support Care Cancer. 2000;8:311-3; J Pain Symptom Manage. 2005;29:344-51; Palliat Med. 2006;20:617-22.) Thus, holistic care that encompasses physical, psychosocial and spiritual aspects can relieve physical symptoms and psychosocial–spiritual distress at the end stage of life for these patients.

(3) However, some of the symptoms, notably pain, did not go away in one week. To seek a better way for pain relief, we attempted to investigate the time-dependent (one week after admission) relationship between pain and psychological & spiritual distress in this study.

(4) The mean survival of all patients admitted to our unit was about 2-3 weeks. Our studies showed us that several symptoms of our patients worsened 48 hours before death, which might result from their rapid deterioration in physical condition (ref: Support Care Cancer. 2000;8:311-3; Palliat Med. 2006;20:617-22.). In addition, only 63 patients were consciously clear enough to report symptoms two weeks after admission in this study. Among the 63 patients, there were only 6 patients with improving pain score. Therefore, we could not analyze this badly censored data.

2. Mental health, major depression (genetics & epigenetics), threat of pain or pain with present day knowledge of fMRI & neurotransmitters, very little is mentioned.

Reply & Revision: We have added a few references on genetic and neuroimaging studies to support our results and enrich discussion. (Please see page 13, line 13-18)

3. The concept of "total pain" is mentioned in passing and requires proper reference material.

Reply & Revision: We have explained the concept of total pain and cited several related references. (Please see page 15, line 1-3)

4. If it an observational study; mixed group of patients including survival 4 days to over year and half, the statistical application and assumptions are not a good fit in my opinion.

Reply & Revision: Thanks for your reminding. We rechecked our data and the median survival was 22.5 days (ranging from 7 to 418 days). All patients admitted to our unit were advanced cancer patients, not responsive to any cancer therapy provided by oncologists. We have revised the text. (Please see page 7, line 2-3) In this study, we focus on the time-dependent (one week after admission to a palliative care unit) relationship between pain and psychological & spiritual distress. Moreover, the survival is not different between the “improved” and “not improved” groups. Thus, the survival time may not be a significant confounding factor.

Reviewer #2: This is a very interesting study and certainly an important one given how inadequate pain management can have such a profound impact on cancer patients at the end of life. It clearly builds on an important program of work. The aim of this prospective longitudinal study was to examine the longitudinal relationship between pain management and psychosocial spiritual distress in advanced cancer patients admitted to a palliative care unit.
Major concerns/revisions

1. The use of the word 'longitudinal' in the title might be a little misleading as there is only one further data collection point, one week after admission. Whilst all prospective observational studies could be called longitudinal I am not sure you really did look at a longitudinal relationship. This requires clearer clarification. My concern also extends to your conclusions in relation to this.

Reply & Revision: Thanks for your comments. We have changed the 'longitudinal' to 'time-dependent', which may be more appropriate. Please see the revised text.

2. Limitations: It might be seen that the measurement of pain on a numerical rating scale was a limitation as pain is a multidimensional experience which you mention in the paper. Did you consider using a multidimensional tool such as the Melzack Pain Questionnaire (MPQ)? This might have given more information related to the components of pain e.g. cognitive or affective and not just the sensory or physical dimensions. Also does a numerical score equal a measure of 'pain management'? Pain assessment and documentation, medication, administered, and comfort strategies might also have been measured to indicate how pain was being managed.

Reply & Revision: A multidimensional tool is indeed better than a numerical rating scale in pain assessment. We have acknowledged this by adding the limitation in the section of discussion. (Please see page 15, line 13-16)

3. In the conclusion I would suggest that your results would also support the recommendation that the routine assessment of psychological distress factors should be encouraged.

Reply & Revision: Thanks for your comment. We have revised our conclusion as your suggestion. (Please see page 15, line 20-21)

Minor revisions

4. In the background please could you clarify the difference between emotional distress and psychosocial spiritual distress. These terms are used interchangeably but not clearly defined

Reply & Revision: Thanks for your reminding. We replaced “emotional” with “psychosocial spiritual” in the revised manuscript.

5. The selection of participants (?inclusion criteria) was based on levels of consciousness. Please give further details of this tool and how it was used.

Reply & Revision: We have defined the levels of consciousness in more detail in the revised manuscript. (Please see page 7, line 5-8)
6. Participants were consecutively enrolled in the study as they were admitted to the palliative care unit. How many were approached and how many declined?

Reply & Revision: We approached 560 patients/or family during the study period, among whom 531 patients/or family participated in the study. However, only 237 patients met the inclusion criteria in the analysis.

7. The methods section relies heavily on previous studies to endorse the selection of measurement tools. These might be described more fully for the reader not familiar with them.

Reply & Revision: We have described the measurement tools in more details. (Please see page 8, line 8-10)

8. How was the cut-off for 'improved' and 'not improved' determined?

Reply & Revision: We described the cut-off for 'improved' and 'not improved' groups in the section of Method. (Please see page 9, line 9-11) Improved: the subjective pain score reported at “one week after admission” is lower than the reported score at “admission”. Not Improved: the subjective pain score reported at “one week after admission” is higher or equal to the reported score at “admission”.

Reviewer #3:

1. Paper is well written and the statistical analysis is appropriate.

Reply & Revision: Thanks for your encouragement.

2. In abstract, there is a sentence saying: 'Consistent with this, a statistically significant interaction between pain and depression scores indicated that pain improvement was dependent on depression amelioration'. This sentence is NOT correct, it should be written as: 'Consistent with this, for depression scores, there is a statistical significant pain group by time interaction effect detected, which means that the pain group effect on depression scores was dependent on time'.

Reply & Revision: Thanks for your revision. We have revised our manuscript. (Please see page 3, line 18-21)

3. Line no. 7 -p9 and line no. 14-p10 mentioned about 'mixed designed ANOVA', I think they are referring to 'one between subject factor-pain group' and 'one within subject factor-time'. It is very unclear.
Reply & Revision: Yes, we are referring to 'one between subject factor-pain group' and 'one within subject factor-time'. We changed the wording as "a mixed designed ANOVA, with one between subject factor-pain group and one within subject factor-time, was used to ... ". (Please see page 9, line 14-15) (Please see page 10, line 21)

4. In this article, it doesn't mention about missing values of the outcome variables. Did every patient complete the whole survey on each time point without missing any questions?

Reply & Revision: Yes, there were some random missing values in our study. We add N in all tables in order to provide related information. (Please see all tables)

5. Please see my modification on table 1.

Reply & Revision: We have revised the table 1 as your modification.

6. Please see my modification on table 2.

Reply & Revision: We have revised the table 2 as your modification.

7. Please see my modification on table 3.

Reply & Revision: We have revised the table 3 as your modification.

8. Please see my modification on table 4.

Reply & Revision: We have revised the table 4 as your modification.