Author's response to reviews

Title: Percutaneous balloon kyphoplasty for the vertebral compression fractures

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Author's response to reviews: see over
Dear Editor,

Submitted please find our article entitled " Percutaneous balloon kyphoplasty for the treatment of vertebral compression fractures" which we are submitting for publication in " BioMedCentral Surgery ". All the manuscript and figures were submitted electronically.

We thank the editor and the reviewers for all of the kind concerns and valuable comments. The manuscript has been rewritten accordingly. Based on the reviewer’s recommendation, we list below in detail the revisions that have been made in response to each concern of reviewer.

We also thanks for Zhiyong Hou and Yingze Zhang for the kind appreciation of our work. We list below in detail our responses to Dr. Georg Osterhoff’s comments.

Reviewer Georg Osterhoff ’s comment 1 :
Throughout the manuscript, I suggest spelling out numbers from one two twelve when stated in a sentence (except decimals and percentages); e.g. “three leakages” instead of “3 leakages”.

Authors’ response:
The numbers have been changed accordingly.(Page.2 to Page. 14)

Reviewer Georg Osterhoff ’s comment 2 :
I am not sure if a difference of .01 degrees of kyphotic correction or of .01 in scores like the VAS or ODI are clinically relevant. Round all numbers in the manuscript to maximum one decimal place (except p-values). Omit “0” in numbers like “0.05” (-> “.05”).

Authors’ response:
Word changed as Reviewer’s suggestion. (Page.2 to Page. 24, including Table 3)

Reviewer Georg Osterhoff ’s comment 3 :
Title: I suggest “Percutaneous balloon kyphoplasty for the treatment of vertebral compression fractures”.

Authors’ response:

Title changed as Reviewer’s suggestion.(Page.1 ,Line 1)

Reviewer Georg Osterhoff’s comment 4:

Abstract:

The Abstract of the manuscript should not exceed 350 words.

Adapt the abstract according to the suggestions made in the sections below.

Authors’ response:

Abstract changed as Reviewer’s suggestion.(Page.2-3, 343 words)

Reviewer Georg Osterhoff’s comment 5:

Background: page 5, line 7, “which can be attributed to pseudarthrosis…kyphoscoliosis”:

Please provide reference.

Authors’ response:

Reference was added (Reference 1, Page 4, Line 9)

Reviewer Georg Osterhoff’s comment 6:

Background: page 5, line 14, “…bed rest, external fixation, and/or…”: Please define “external fixation”. By corset?

Authors’ response:

external fixation such as brace or corset. Sentence added as reviewer’s suggestion (Page 4, Line 14-15)

Reviewer Georg Osterhoff’s comment 7:

page 5, line 17: as well as thromboembolic complications and pneumonia!

Authors’ response:
Reviewer Georg Osterhoff’s comment 8:

Methods: The description of patient inclusion/exclusion is imprecise. Was inclusion done consecutively? How many patients were included? How many were excluded? If 187 patients were operated between 2011 and June 2012, how is it possible that 187 patients were analyzed?

Authors’ response:

1. The inclusion criteria were (1) focal midline back pain managed inadequately with appropriate conservative treatment, (2) back pain related to VCF location on radiography, and (3) presence of bone marrow edema on magnetic resonance imaging and exclusion criteria were active infection and uncorrected therapeutic anticoagulation.

2. Vertebroplasty and kyphoplasty were performed in about four hundred patients per year. Kyphoplasty was favored in the presence of kyphotic deformity which contribute significantly to morbidity and disruption of the posterior vertebral cortex, where high-viscosity cement can be delivered.

3. Clinical follow-up examination of the patients was independently performed by an orthopedic specialist, and diagnostic images were independently evaluated by a radiologist.

Reviewer Georg Osterhoff’s comment 9:

Methods: How long was the median follow-up (and range)? In Table 1 the authors state that four patients were lost to follow-up; when?

Authors’ response:

183 patients finished one year follow-up and four patients were lost to follow-up in first 3 months.
Table 1 was revised. (Page22, Table1)

**Reviewer Georg Osterhoff’s comment 10:**

**Methods:**

Seventy-nine percent of the patients have a follow-up of less than 12 months!

This is a key limitation of the study and is not even mentioned in the discussion.

**Authors’ response:**

183 patients finished one year follow-up till June 2013. The radiographic and clinical data were revised in Table 3 and sentence in text. (Page10, Line 1) (Page22, Table3)

**Reviewer Georg Osterhoff’s comment 11:**

**Methods:** page 6, line 18: Provide IRB approval reference number.

**Authors’ response:**

Thanks for your kindly reminding. IRB approval reference number (101-3955B) was provided. (Page5, Line 19)

**Reviewer Georg Osterhoff’s comment 12:**

**Methods:** page 7, line 9: “The study was … board”: This was mentioned before (page 6, line 18).

**Authors’ response:**

Sentence deleted as reviewer’s suggestion.

**Reviewer Georg Osterhoff’s comment 13:**

**Methods:** page 8, line 6: “unilaterally”: It is interesting that you achieved such a good kyphotic correction by the use of only one balloon. Did you inflate/deflate the balloon in several positions to gain symmetric angular restoration? As stated in Table 2, three vertebrae were approached bipedically. Please add in the Methods section and explain why you did this in some cases.

**Authors’ response:**
Unilateral extrapedicular approach was used in 184 patients to allow central placement of the balloon in the vertebral body to achieve a good kyphotic correction by the use of only one ballon. If unilateral extrapedicular approach can not achieved, bipedicular was done in order to gain symmetrical angular restoration .Table 2 was revised (Page23, Table2)

**Reviewer Georg Osterhoff’s comment 14:**

Methods: page 8, line 13: As stated by the authors in the discussion section, the viscosity of the cement is of great importance. How was viscosity determined or estimated before injection?

**Authors’ response:**

The viscosity was influenced mainly by temperature at operation room during polymerization. The low-viscosity cement defined as a runny liquid form while high-viscosity cement as a nearly dough like state. High-viscosity cement was applied in our series.

**Reviewer Georg Osterhoff’s comment 15:**

Methods: page 8, line 17: There is a verb missing in this sentence

**Authors’ response:**

Parameters related to imaging and technical characteristics, including approach method, amount of bone cement injected, local or general anesthesia applied.

( Page8 ,Line3 )

**Reviewer Georg Osterhoff’s comment 16:**

Methods: page 8, line 19: The authors use different terms to describe the kyphotic deformation/correction: “kyphosis angle”, “kyphotic angle” or “Cobb angle”.

Adhere to one term throughout the manuscript and define precisely how it was measured (e.g. endplate-to-endplate of the fractured vertebrae).
Authors’ response:

Kyphosis angle and Cobb angle were changed to kyphotic angle which was defined as the Cobb angle measurements taken from the superior endplate of the vertebra one level above the treated vertebra to the inferior endplate of the vertebral body one level below the treated vertebra on the lateral X-ray image. (Page 8, Line 4-7 and Figure 3)

Reviewer Georg Osterhoff’s comment 17:

Methods: page 9, line 1: How was leakage assessed? By radiographs or by CT scans?

Authors’ response:

Patterns of cement leakage were assessed by radiographs using the classification…defect. (Page 8, Line 9)

Reviewer Georg Osterhoff’s comment 18:

Methods: page 9, line 8: How is this possible if some patients were operated in June 2012 (invitation for this review was made in May 2013)?

Authors’ response:

All patient received operation for one year till June 2013 and time from kyphoplasty to latest follow-up in Table 1 and data of post-op month 12 in Table 3 were revised. (Page 10, Line 1) (Page 22, Table 1 and Page 24, table 3)

Reviewer Georg Osterhoff’s comment 19:

Methods: page 9, line 13: The SF-36 was not mentioned before in the Methods section, no results are given in the Results section…

Authors’ response:

Means were calculated for different variables, including scores on the ODI, and VAS, ...body. SF-36 in statistical analysis of method was deleted. (Page 9, Line 3-5)

Reviewer Georg Osterhoff’s comment 20:

Methods: page 9, line 16: Did you adjust for multiple comparisons?
Authors’ response:

The t test was used to compare the data between per-operative and each post-operative subgroups. No other adjustment methods were applied.

Reviewer Georg Osterhoff’s comment 21:

Results: Round all numbers in the manuscript to maximum one decimal (except p-values).

Authors’ response:

Words changed as reviewer’s suggestion. (Page2-24)

Reviewer Georg Osterhoff’s comment 22:

Results: page 10, line 5: Provide precise p-values (<.05 is not sufficient).

Authors’ response:

Precise p-values were added. (Page9, Line12, Line15 and Page 10, Line 7,8,10)

Reviewer Georg Osterhoff’s comment 23:

Results: page 10, line 5 ff: Use “°” and “%” for all the numbers before and after the “±” (as correctly done in line 4).

Authors’ response:

Words changed as reviewer’s suggestion. (Page9, Line11-15)

Reviewer Georg Osterhoff’s comment 24:

Results: page 10, line 5, “to 8.21±0.85 at last follow-up”: Last follow-up would be defined as the last follow-up of an individual patient (and therefore include data of ALL251 vertebrae in 187 patients minus those lost to follow-up = xxx vertebra in 184 patients). The number “8.21±0.85” given in the text, however is the value given for the “Post-op month 12” in Table 3 (and therefore includes only those vertebrae in the 39 patients with a follow-up of 12 months (Table 1). The same accounts for the value given in the text for “last follow-up” of anterior vertebral
height. Please clarify.

Authors’ response:

All patient received operation for one year till June 2013 and time from kyphoplasty to latest follow-up in Table 1 and data of post-op month 12 in Table 3 were revised. Radiographic measurement ... follow-up. (Page9,Line10-14,and Page 22,Table 1 and Page 24,table 3)

Reviewer Georg Osterhoff’s comment 25:

Result:page 10, line 6: Fifty-two percent of what? How was 100% anterior vertebral height defined?

Authors’ response:

Anterior Vertebral height is expressed as fractions of referent vertebral height (AVH= Anterior Vertebral height of index fractured vertebrae/average of above and below intact anterior vertebral height) (Page 24,table 3)

Reviewer Georg Osterhoff’s comment 26:

Result:page 10, line 17: Suggest “patients”.

Authors’ response:

The orthopedic balloon ruptured in two patients....consequences.

Words changed as reviewer’s suggestion. (Page10,Line12)

Reviewer Georg Osterhoff’s comment 27:

Result:page 11, line 3+4: Suggest “leakages”

Authors’ response:

Words changed as reviewer’s suggestion. (Page10,Line16,17)

Reviewer Georg Osterhoff’s comment 28:

Result:Did you have any other peri- and postoperative complications?

Authors’ response:

No patients suffered neurological deficits,symptomatic pulmonary embolism or
post-operative infection.

Sentence added as reviewer’s suggestion. (Page10,Line18 to Page101,Line1)

Reviewer Georg’s comment 29:

Result: Six patients with fractures due to malignancies (Table 1, metastasis 1, MM 5) were included. Did you observe differences in the clinical outcome (ODI/VAS) at 12 months when compared to the osteoporotic patients?

Authors’ response:

No differences in the clinical outcomes (ODI/VAS) were observed at 12 months of follow-up. Thanks for your kind reminder.

Reviewer Georg Osterhoff’s comment 30:

Discussion: I would suggest to less describe what is already known and to focus on specifically discussing the results of this study with the current literature.

Restructure the discussion as follows: 1. reiterating the purpose and the major two or three findings of the study. 2. compare and contrast these with available evidence. 3. discuss the limitations of the study (e.g., strengths and weaknesses, etc.). 4. discuss areas for future study and research. 5. give a clinical message.

Authors’ response:

1. In addition to the available evidence, the benefits of balloon kyphoplasty based on our results included better spinal alignment restoration and less cement extravasation than those in vertebroplasty (Reference 15,24-30).(Page12,Line 5-9)
2. In our series, the mean VAS score and ODI score improved significantly from 7.7±1.3 to 0.5±0.1 and from 56.8±4.2 to 12.5±1.6, respectively, at one year of follow-up. The long-lasting pain relief provided by balloon kyphoplasty can be attributed to the improved sagittal profile of the spine, which results in a lower compensating activity of the muscles (Reference 27,31). (Page12,Line9-13)
3. The present study had limitations including its small number of patients and short follow-up period. The limited number of patients in this study possibly affects the statistical power and a long-term follow-up would be required to further evaluate the efficacy of this procedure. Our follow-up is only 12 months, which most authors consider to be a short-term period. However, the high rates of comorbidities and mortality related to elderly populations may make long-term follow-up infeasible. (Page 13, Line 16-19)

4. We are currently gathering 2-year follow-up data from additional patients treated at our institution, but future prospective randomized studies with a large patient enrollment are needed to validate our findings. (Page 14, Line 4-6)

**Reviewer Georg Osterhoff’s comment 31:**

Discussion: page 13, line 10: Werner et al (J Bone Joint Surg Am. 2013;95:577-84) reported cement leakage rates of 25% when assessed by CT scan. How did you assure not to miss a leakage?

Authors’ response:

In our study, asymptomatic cement extravasation occurred in an average of 11.5% of the vertebrae treated, which is considerably lower than that observed in vertebroplasty. Cotten A et al (Radiographics 1998;18:311-20), Deramond H et al (Radiol Clin North Am 1998;36:533-546), and Garfin SR et al (Spine 2001;26:1511-1515) describe their leakage rate of vertebroplasty is around 30-67% in X-ray. Maybe some leakages will miss without CT scan, but we compared with vertebroplasty in X-ray.

**Reviewer Georg Osterhoff’s comment 32:**

Discussion: page 13, line 11-15: This was not investigated by the submitted study.

Authors’ response:
Compared with previous studies[9,24,26], this finding supports... vertebrae.

Sentence changed as reviewer’s suggestion. (Page13,Line10)

Reviewer Georg Osterhoff’s comment 33:

Conclusion: page 13, line 18, “less”: less than what?

Authors’ response:

....less bone cement leakage than vertebroplasty.

Sentence changed as reviewer’s suggestion. (Page 14, Line 9)

Reviewer Georg Osterhoff’s comment 34:

Conclusion: page 13, line 18, “We conclude that compared with nonsurgical management...”:

This conclusion cannot be drawn based on the data provided by the submitted study, there was no control-group.

Authors’ response:

compared with nonsurgical management was deleted. (Page 14, Line 9)

Reviewer Georg Osterhoff’s comment 35:

Conclusion: page 14, line 2, “…in our 12 months follow-up”: I would be very careful with this conclusion as most of the patients had a follow-up of less than 12 months.

Authors’ response:

183 patients finished one year follow-up till June 2013.( Page 10, Line 1 and Page 22, Table 1)

Reviewer Georg Osterhoff’s comment 36:

page 14, line 2, “The treatment of VCFs with balloon kyphoplasty...”: I totally agree with this conclusion.

Authors’ response:
Thank you for your appreciation.

**Reviewer Georg Osterhoff’s comment 37:**

Figures & Figure legends:

Figure 1-6: The procedure of BKP is well known. I would suggest to omit Figure 1+2, to merge Figure 4-5 and to shorten the Figure legends accordingly.

You might provide a Figure that shows the technique of kyphotic angle measurement.

**Authors’ response:**

The figures have been modified accordingly.

**Reviewer Georg Osterhoff’s comment 38:**

Tables: Tables were commented above. Provide “n” in the columns of Table 3.

**Authors’ response:**

The tables have been revised as you suggested.

Your Sincerely,

Sincerely,

Lih-Huei Chen, M.D.
Chief and Professor
Spine section, Department of Orthopaedics
Chang Gung Memorial Hospital and Chang Gung University