Journal of Clinical and Translational Research
Peer review process file 09.202302.005

Percutaneous pedicle screw fixation combined with percutaneous vertebroplasty for the treatment of thoracic and lumbar metastatic tumors

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Review timeline:

Received: 8 November, 2022
Editorial decision: 6 December, 2022
Revision received: 2 January, 2023
Editorial decision: 2 January, 2023
Published online: 14 February, 2023

1st Editorial decision
06-Dec-2022

Ref.: Ms. No. JCTRes-D-22-00193
New option:Percutaneous pedicle screw fixation combined with percutaneous vertebroplasty for the treatment of thoracic and lumbar metastatic tumours
Journal of Clinical and Translational Research

Dear Dr. Feng,

Reviewers have now commented on your paper. You will see that they are advising that you revise your manuscript. If you are prepared to undertake the work required, I would be pleased to reconsider my decision.

For your guidance, reviewers' comments are appended below.

If you decide to revise the work, please submit a list of changes or a rebuttal against each point which is being raised when you submit the revised manuscript. Also, please ensure that the track changes function is switched on when implementing the revisions. This enables the reviewers to rapidly verify all changes made.

Your revision is due by Jan 05, 2023.

To submit a revision, go to https://www.editorialmanager.com/jctres/ and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely

Michal Heger
Editor-in-Chief
Journal of Clinical and Translational Research

Reviewers' comments:

Reviewer #1: The author report 40 cases with thoracic and lumbar metastatic tumor, the result is good.
There are several questions:
1 How did the doctor choose these 40 patients , by time, or by symptoms, it's a random choose or not, the including criteria in the paper is not enough?
2 Why these patients use PPST+PVP fixation , in lots of paper , PVP also gets good result , PPST increase the patients hospital expense.
3 For these patients , will PVP accelerate the tumor cell transfer to other organization

Reviewer #2:
MAJOR:

1. The language needs considerable revision. Please engage a native speaker who is well-versed in the subject matter, contract a third-party editing service, or contact the editorial office (m.heger@jctres.com) for assistance with language editing and content appraisal. Please note that the latter two services will incur a fee. Some sentences are very unclear and do not relay the underlying meaning properly. For example, "Pathological examination was performed on tissue samples from the diseased vertebra to evaluate the relationship between the diseased vertebral tissue and the primary disease" probably intends to indicate that pathological examination was conducted to ascertain the origin of the lesion (i.e., determine the primary site of the malignancy).
2. Indicate in the Methods section that this was a prospective trial and include a CONSORT flow chart as Figure 1.
3. In the Introduction the authors clarify that the study was performed to assess the feasibility, effectiveness, and safety of the combined PVP and PPSF technique. The authors must explicitly state in the text how feasibility, effectiveness, and safety were concretely and objectively assessed.
4. The type of neoadjuvant therapy (radiotherapy, chemotherapy) as well as number of treatments received and dosage should be specified for each case.
5. The Kaplan-Meier plot for OS (Figure 2D) should also be stratified according to the site of primary malignancy. The survival can then be presented in a separate figure.
6. Patient demographics and medical information of the cohort are missing and should be added in a separate table.
7. The authors must provide a clear scientific rationale for clustering the analysis of vertebral metastases that have different origins of the primary tumor. A good argumentative foundation for the clustering can be found here: https://pubmed.ncbi.nlm.nih.gov/30658673/.

8. In the Results section, the authors state that the operations were successful. However, in the Methods section no definition was provided for a successful operation. What were the predefined criteria that would be used to deem an operation 'successful'? The same applies to the outcome parameters internal fixation (what constitutes satisfactory?) and PMMA dispersion (what constitutes good PMMA dispersion?).
9. In Figure 2A (VAS) and 2B (BIADL) the scores are provided for 20 cases, while the cohort consisted of 40 patients. Please explain this discrepancy.
10. The data in Figure 2A and B should be plotted as dot plots with superimposed mean and standard deviation for each measurement time point (not as continuous data as suggested by the lines).
11. The current results should be juxtaposed to similar outcome parameters but for individual interventions (so PVP + PPSF compared to PVP alone and PVP + PPSF compared to PPSF alone), where the data for the individual treatments are obtained from the authors' own database and/or published work. Only this will justify your position that "We believe that PPFS combined with PVP is an effective treatment for thoracic and lumbar metastatic tumours, which can ease the pain of the patients and improve their quality of life." Your conclusions should be aligned with the aims of the study. It should be unequivocal why the combined regimen is superior to the singular regimens.

MINOR:

1. The ethics approval and informed consent statement should be placed in the Methods section. Also, please supply the IRB number associated with the approval.
2. The figures should be resized to 6 inch width and at least 300 dpi resolution to augment legibility.
3. The data in Table 1 do not have to be repeated in the text (i.e., types of primary malignancy).
4. All abbreviations in the main text must be written out at first mention.
4. Shortly detail in the Methods section what the Tomita and Tokuhashi scoring systems measure, and how the scores should be interpreted. Not every reader will be familiar with the niceties of these scoring systems.

Authors' response

Dear Editors

We appreciate the reviewers' comments which have helped us significantly improve the scientific quality of this manuscript. Here are the point-to-point responses to reviewers' comments below.

Helin Feng
Department of Orthopedics, The Fourth Hospital of Hebei Medical University
On behalf of all authors.

Reviewer #1:

1) How did the doctor choose these 40 patients , by time, or by symptoms, it's a random choose or not, the including criteria in the paper is not enough?

RESPONSE: Thank you for your suggestions. This is a retrospective study. Patients were screened according to time. We added that in the **Population Data**.

"**Population Data**
The radiologic and clinical data of patients with multi-segmental thoracolumbar metastases treated with PVP combined with PPSF in our hospital between January 2019 and December 2021 were retrospectively analyzed. This case series included 40 patients with thoracic and lumbar metastatic tumours."

2 Why these patients use PPST+PVP fixation , in lots of paper , PVP also gets good result , PPST increase the patients hospital expense.

RESPONSE: Spinal metastasis is a common disease. As the life expectancy of cancer patients increases, the number of patients with spinal metastases is expected to increase. Patients with osteolytic spinal metastases experience severe pain, which can significantly reduce the quality of life. Open surgery is highly risky and is not suitable for cancer patients with severe comorbidities and poor general condition. Therefore, the current treatment mode for patients with spinal metastases has turned to minimally invasive treatment. There are many minimally invasive treatment options for spinal metastases, such as vertebroplasty, vertebral augmentation, and coblation and radiofrequency ablation systems. There are no specific techniques that have proven to be most appropriate for the treatment of spinal metastases, so treatment often depends on operator and/or institution-based preferences or bias. As you mentioned, PVP has been widely used in the treatment of vertebral metastases, but the relationship between spinal stability and PVP treatment has not been reported in the previous literature. In this article, we highlight that vertebral metastases involve multiple segments and SINS scores range from 9 to 16, with osteolytic destruction of the vertebral body extending over half of the vertebral body. Therefore, the purpose of combining PPSF on the basis of PVP is to further strengthen the stability of the spine. We performed the surgery with respect for the patients and their families, and in order to further clarify our presentation, we have added relevant content in the text.

"Before the procedure, all participants signed a detailed consent form describing the benefits and risks of the procedure, including but not limited to: PPSF increases the cost of the procedure but may have a modest effect, etc. The review board at our hospital did not require further approval for the use of patient records and images."

3 For these patients , will PVP accelerate the tumor cell transfer to other organization

RESPONSE: PVP is one of the effective treatments for spinal metastases, and it has not been reported that PVP promotes the metastasis of tumor cells to other tissues.

Reviewer #2:

MAJOR:

1. The language needs considerable revision. Please engage a native speaker who is well-versed in the subject matter, contract a third-party editing service, or contact the editorial office (m.heger@jctres.com) for assistance with language editing and content appraisal. Please note

that the latter two services will incur a fee. Some sentences are very unclear and do not relay the underlying meaning properly. For example, "Pathological examination was performed on tissue samples from the diseased vertebra to evaluate the relationship between the diseased vertebral tissue and the primary disease" probably intends to indicate that pathological examination was conducted to ascertain the origin of the lesion (i.e., determine the primary site of the malignancy).

RESPONSE: Thanks for your suggestion, we have revised these sentences. We have refined the text and we will upload the proof afterwards.

2. Indicate in the Methods section that this was a prospective trial and include a CONSORT flow chart as Figure 1.

RESPONSE: Thank you for your suggestions, which we have supplemented in the Methods section.

"**Population Data**
The radiologic and clinical data of patients with multi-segmental thoracolumbar metastases treated with PVP combined with PPSF in our hospital between January 2019 and December 2021 were retrospectively analyzed. This case series included 40 patients with thoracic and lumbar metastatic tumours. The inclusion criteria were as follows: (1) pathological fractures of the thoracolumbar vertebral body caused by tumour bone metastasis confirmed by postoperative pathology, (2) no spinal cord or nerve injury confirmed by CT and MRI, and no obvious spinal canal occupation, and (3) preoperative SINS score was 7-12, and there was a lesion in the posterior column of the vertebral body, or preoperative SINS score of 13-18. The exclusion criteria were as follows: (1) absolute contraindication for surgery, for example, severe cardiopulmonary dysfunction, coagulopathy, poor basic condition, or unable to tolerate an operation; (2) pathological fractures due to reasons other than tumour destruction, such as osteoporosis; and (3) neurological symptoms or intraspinal space-occupying, indicating a significant need for decompression. Prior to surgery, all participants signed a detailed consent form describing the benefits and risks of the procedure and our hospital review board did not require further approval for the use of patient records and images."

3. In the Introduction the authors clarify that the study was performed to assess the feasibility, effectiveness, and safety of the combined PVP and PPSF technique. The authors must explicitly state in the text how feasibility, effectiveness, and safety were concretely and objectively assessed.

RESPONSE: In our report, all 40 patients were treated with PVP combined with PPSF, and the operation was very successful. All the patients who underwent X-ray examination after the operation, which showed that the internal fixation was in good position, there was no leakage of bone cement, and the bone cement was packed at the site of lytic destruction in the vertebral body. No surgery-related complications occurred in all patients. The VAS scores of all patients were significantly decreased and the BIADL scores were significantly increased after operation. This result showed significant pain relief and improved quality of life after PVP combined with PPSF. Therefore, in general, PVP combined with PPSF is safe in the treatment of multilevel vertebral metastasis, which can achieve satisfactory clinical results for patients and clinicians, and significantly improve the quality of life of patients. We supplemented it in the discussion section based on your comments.

"DISCUSSION
In recent years, with the development of comprehensive tumour therapy, the extension of survival time of tumour patients and the widespread use of MRI, the remedy of spinal metastasis has become a common clinical issue. In the meantime, with the development of remedies for spinal metastases and the improvement of spinal surgery techniques, surgery has become one of the main approaches to spinal metastases. This study incorporated 40 patients, all of whom underwent PPSF combined with PVP after a detailed preoperative evaluation. All patients successfully completed the operation. All patients underwent postoperative X-ray examination, which showed that the position of the internal fixation was good, there was no leakage of bone cement, and the bone cement was filled in the location of osteolytic destruction in the vertebral body. No surgery-related complications occurred in all patients. The VAS scores of all patients were significantly decreased and the BIADL scores were significantly increased after operation. This result showed significant pain relief and improved quality of life after PVP combined with PPSF. Therefore, in general, PVP combined with PPSF is safe in the treatment of multilevel vertebral metastasis, which can achieve satisfactory clinical results for patients and clinicians, and significantly improve the quality of life of patients."

4. The type of neoadjuvant therapy (radiotherapy, chemotherapy) as well as number of treatments received and dosage should be specified for each case.

RESPONSE: In this article, we aim to introduce new surgical options for patients with multilevel spinal metastases with a highly unstable spine. Postoperative patients will receive standardized chemoradiotherapy or targeted therapy in the corresponding clinical departments according to the patient's condition.

5. The Kaplan-Meier plot for OS (Figure 2D) should also be stratified according to the site of primary malignancy. The survival can then be presented in a separate figure.

RESPONSE: The purpose of our study is to provide a new surgical option for patients with bone metastases based on the condition of spinal lesions, spinal stability, and spinal cord injury assessment. The location of the primary malignant tumor has little influence on the choice of surgical plan. Therefore, we agreed that retaining the current Kaplan-Meier plot (Figure 2D) was the best option.

6. Patient demographics and medical information of the cohort are missing and should be added in a separate table.

RESPONSE: Thank you for your suggestions, and we have supplemented them according to your suggestions.

7. The authors must provide a clear scientific rationale for clustering the analysis of vertebral metastases that have different origins of the primary tumor. A good argumentative foundation for the clustering can be found here: https://pubmed.ncbi.nlm.nih.gov/30658673/.

RESPONSE: We have carefully studied the article you shared and found that sex, Karnofsky performance status, primary site, visceral metastasis and other indicators are important predictors of survival in patients with bone metastases. We should note that our use of the spinal stability and spinal cord injury assessment System (including Tomita score, Modified Tokuhashi Scoring System and SINS) has included consideration of these factors. The details

of each scoring system will be supplemented in the article. The article you shared is also a good hint and help for our research, and we have cited it in the article, the citation number is 12.

8. In the Results section, the authors state that the operations were successful. However, in the Methods section no definition was provided for a successful operation. What were the predefined criteria that would be used to deem an operation 'successful'? The same applies to the outcome parameters internal fixation (what constitutes satisfactory?) and PMMA dispersion (what constitutes good PMMA dispersion?).

RESPONSE: Thank you for your correction, and we have supplemented the details in the results section.
"RESULTS
All operations were successfully completed. There were no puncture injury, spinal cord or nerve root compression symptoms, intraspinal hemorrhage during operation, and no serious complications such as infection and pulmonary embolism after operation. All patients underwent postoperative X-ray examination, which showed that the position of the internal fixation was good, there was no leakage of bone cement, and the bone cement was filled in the location of osteolytic destruction in the vertebral body."

9. In Figure 2A (VAS) and 2B (BIADL) the scores are provided for 20 cases, while the cohort consisted of 40 patients. Please explain this discrepancy.

RESPONSE: Thanks for the critic, We have corrected the error.

10. The data in Figure 2A and B should be plotted as dot plots with superimposed mean and standard deviation for each measurement time point (not as continuous data as suggested by the lines).

RESPONSE: Thanks for your suggestion, we have modified the chart according to your suggestion.

11. The current results should be juxtaposed to similar outcome parameters but for individual interventions (so PVP + PPSF compared to PVP alone and PVP + PPSF compared to PPSF alone), where the data for the individual treatments are obtained from the authors' own database and/or published work. Only this will justify your position that "We believe that PPFS combined with PVP is an effective treatment for thoracic and lumbar metastatic tumours, which can ease the pain of the patients and improve their quality of life." Your conclusions should be aligned with the aims of the study. It should be unequivocal why the combined regimen is superior to the singular regimens.

RESPONSE: Thanks for your suggestion. This is good advice. Here, we would like to note that PPSF alone is mostly suitable for vertebral compression fractures or vertebral burst fractures caused by trauma, and PPSF alone is not recommended for patients with spinal metastases. In addition, compared with PVP, PVP combined with PPSF is suitable for patients with multi-segmental thoracolumbar metastatic tumors with high spinal instability score and osteolytic destruction of the vertebral body more than half of the vertebral body. Different treatment measures are used for different patients, so PVP + PPSF should not be compared with PVP alone.

MINOR:

1. The ethics approval and informed consent statement should be placed in the Methods section. Also, please supply the IRB number associated with the approval.

RESPONSE: We have supplemented this in the Methods section.

"**Population Data**
The radiologic and clinical data of patients with multi-segmental thoracolumbar metastases treated with PVP combined with PPSF in our hospital between January 2019 and December 2021 were retrospectively analyzed. This case series included 40 patients with thoracic and lumbar metastatic tumours. The inclusion criteria were as follows: (1) pathological fractures of the thoracolumbar vertebral body caused by tumour bone metastasis confirmed by postoperative pathology, (2) no spinal cord or nerve injury confirmed by CT and MRI, and no obvious spinal canal occupation, and (3) preoperative SINS score was 7-12, and there was a lesion in the posterior column of the vertebral body, or preoperative SINS score of 13-18. The exclusion criteria were as follows: (1) absolute contraindication for surgery, for example, severe cardiopulmonary dysfunction, coagulopathy, poor basic condition, or unable to tolerate an operation; (2) pathological fractures due to reasons other than tumour destruction, such as osteoporosis; and (3) neurological symptoms or intraspinal space-occupying, indicating a significant need for decompression. Prior to surgery, all participants signed a detailed consent form describing the benefits and risks of the procedure and our hospital review board did not require further approval for the use of patient records and images."

2. The figures should be resized to 6 inch width and at least 300 dpi resolution to augment legibility.

RESPONSE: We adjusted the quality of the images.

3. The data in Table 1 do not have to be repeated in the text (i.e., types of primary malignancy).

RESPONSE: Thanks for your suggestion. We have supplemented the relevant content in the article.

4. All abbreviations in the main text must be written out at first mention.

RESPONSE: Thanks for your suggestion. We have supplemented the relevant content in the article.

5. Shortly detail in the Methods section what the Tomita and Tokuhashi scoring systems measure, and how the scores should be interpreted. Not every reader will be familiar with the niceties of these scoring systems.

RESPONSE: The details of each scoring system will be supplemented in the article.

2nd Editorial decision
02-Jan-2023

New option:Percutaneous pedicle screw fixation combined with percutaneous vertebroplasty for the treatment of thoracic and lumbar metastatic tumours
Journal of Clinical and Translational Research

Dear authors,

I am pleased to inform you that your manuscript has been accepted for publication in the Journal of Clinical and Translational Research.

You will receive the proofs of your article shortly, which we kindly ask you to thoroughly review for any errors.
Please notify our assistant editor/production editor when you receive the proofs if your article should belong to a special issue specifying the issue's title.

Thank you for submitting your work to JCTR.

Kindest regards,

Michal Heger
Editor-in-Chief
Journal of Clinical and Translational Research

Comments from the editors and reviewers: