

Reviewer's report

Title: Balloon Kyphoplasty in malignant spinal fractures: A Systematic Review and Meta-analysis.

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Reviewer: Sheena Derry

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Spinal fractures contribute greatly to the suffering of many patients with osteolytic metastasis and multiple myeloma, and it is important to identify the most appropriate treatment options, and gaps in the evidence. I hope my comments will help to improve this paper.

General comments

1. English is not the first language of the authors, and I think there is room to both improve clarity and reduce word count.
2. Methods. Observational studies can be difficult to find by electronic searching [1, 2]. Some people find citation tracking helpful.
3. As in many palliative care treatments, there is a dearth of high quality evidence from large double blind randomised controlled trials. There are many well-documented reasons why it is difficult or impossible to conduct such trials in this population. That should not deter us from examining other evidence, and indeed observational studies can provide equally robust evidence provided criteria of quality, validity and size are met. The authors have clearly tried to assess potential bias from various sources, and comment on the methodological quality of the studies. However, apart from mentioning the "limited number of patients" at the beginning of the discussion, they make no mention of the susceptibility of the included study results to the random play of chance due to small numbers [3].
4. It is unfortunate that the majority of the data for pain relief are presented as population means, which can mask significant differences between individuals. In the two studies for which adequate data are available, most patients do seem to have severe pain at baseline (>6), which is reduced to none or mild (<3) postoperatively. This kind of clinical interpretation gives more meaning than simply saying there was a statistically significant reduction. What matters is how many patients return to a tolerable level of pain, not whether the difference was statistically significant. Similar comments relating to use of mean data and statistical versus clinical significance apply to Functional Capacity, Quality of Life, Vertebral height and Kyphotic angle. The data presented do not tell me what difference the procedure made to the patient. I appreciate, however, that the original studies probably reported only mean data.

Compulsory revisions

1. Abstract

This is a little wordy, but lacks important information. For example:

“Methods: We searched several electronic databases to September 2008, and reference lists of relevant studies for studies of any design that reported on balloon kyphoplasty in patients with spinal fractures secondary to osteolytic metastasis and multiple myeloma. Outcomes sought included pain relief, functional capacity, quality of life, vertebral height, kyphotic angle and adverse events. Studies were assessed for methodological bias, and estimates of effect calculated using random-effects model. Potential reasons for heterogeneity were explored.”

This has a slightly higher word count than the original, but gives a clearer picture of what the review is about, and word count can be reduced in Results and Conclusions.

Results: Claims of efficacy should perhaps be tempered with “in these studies”, since the data is so limited.

2. Background

In the first paragraph the authors state that “spinal fractures significantly increase the risk of new fractures”. Is this true? Or is it the case that those who have had one fracture are already predisposed to fractures, and hence more likely to have another one?

3. Methods

Clinical outcomes sought are poorly described. Did you look for any information on any of these outcomes? If so, did you have prespecified criteria for which were your desired outcomes and/or what a clinically useful outcome would be? For example, did you look for particular validated scales? Did you accept undefined “improvement” in pain, and was pain patient-reported or investigator reported (reduced validity)? The recent IMMPACT consensus statement suggests measures of change in pain and other outcomes that have clinical relevance in chronic pain conditions [4].

4. Results

a. Why were references without abstracts excluded? Please identify the included studies (e.g. “These studies, three retrospective [refs] and four prospective [refs] single-centre...”). One of the studies excluded because of data duplication in subsequent or more complete publications [your ref 24] is cited when reporting details of the patients’ condition (2nd paragraph). Is this a mistake, or did only that publication provide that data?

b. On what basis are the studies described as “representative”?

c. Pain Relief.

- Was pain relief patient-reported? Investigator reported pain estimates frequently do not correlate well with patient reported estimates.

- What is meant by “improvement”? Is it clinically relevant improvement?
- d. Safety. Cement leaks. I question the value and validity of combining these data to give a statistical output, given the small number of events.

5. Discussion

a. The limited nature of the results, in terms of numbers of patients/procedures and outcomes reported should be acknowledged. The fact that they are in broad agreement with those in osteoporotic fractures may give added weight and increase our confidence in them.

b. Paragraph 1. I think “assumptions” is the wrong word. The authors probably mean “conclusions”, although I would not like to draw firm conclusions from this limited data. Perhaps “Nonetheless, combined analysis gives results that are in broad agreement with earlier reports that focussed on osteoporotic fractures”.

c. It would be helpful to state what pain relief value is considered clinically significant in Jensen (ref 38), and also to refer to the recently published IMMPACT recommendations [4].

d. Safety. These studies were not designed to evaluate adverse events, so although the information they provide is useful, and may give insight into potential common events, they cannot evaluate less common, and potentially serious events. This should be acknowledged.

e. Conclusions. Future studies should have consistent reporting of clinically useful outcomes.

Minor revisions

Table 1. Add BKP and VP in footnotes.

Table 2. Functional capacity and Quality of Life: it would help to state the range of the scale used, as is done for VAS. Be consistent with abbreviations for weeks, months, years. State (in footnote?) that continuous data is presented as means \pm SD.

Table 3. Give range for VAS and ODI.

Figure 1. Exclusions do not clearly tie in with the text (paragraph 1 Results).

References

1. Lemeshow AR et al. Searching one or two databases was insufficient for meta-analysis of observational studies. *J Clin Epidemiol* 2005; 58: 867-873
2. Ruppen W et al. Incidence of epidural hematoma, infection, and neurologic injury in obstetric patients with epidural analgesia/anesthesia. *Anesthesiology* 2006;105:394-9.
3. Moore RA et al. Size is everything--large amounts of information are needed to overcome random effects in estimating direction and magnitude of treatment effects. *Pain*. 1998;78:209-16.
4. Dworkin RH et al. Interpreting the clinical importance of treatment outcomes in

chronic pain clinical trials: IMMPACT recommendations. J Pain. 2008;9:105-21.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests