

Peer Review File

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Reviewer A

This is an observational study of the effect of age on patient based on patient demographic and surgical procedures. This is interesting work that further bolsters the idea that elderly (defined as greater than 75 years by the authors) have outcomes measures that are equivalent to younger patients.

It would be advantageous for the authors to state a specific hypothesis for this work rather than an "Aim" (Line 106). This would open the statistical analysis to larger possibilities such as risk analysis for various comorbidities. Such a hypothesis would also explain how it appears that the authors should account for pedicle screw differences, e.g. does the cemented pedicle screw have an effect, or bone quality, e.g. osteoporosis? The direct statement of a hypothesis would also explain the statistical claim on Line 204.

Reply 1: Thanks for the suggestion. We have tried to improve the manuscript according to your comments by introducing the hypothesis that there are no significant differences in clinical and health-related quality of life scores between both groups with the use of implants appropriate for bone density of each group.

Changes in the text: (Page 4: Lines 9-16) "The present study describes the clinical and radiological outcomes, quality of life and functional improvement, as well as the surgically related complications in a group of elderly patients (>75 years of age) who underwent posterior decompression and fusion with cemented PMMA pedicle screw augmentation. We then compare these results with data from a similar procedure carried out in a younger population (<65 years of age) with uncemented instrumentation. We hypothesize that there are no significant differences in clinical and health-related quality of life scores between both groups with the use of implants appropriate for their bone density."

At this point there is confusion with this reviewer as to the exact hypotheses being tested. Did the cemented screws affect outcomes in the older patient? It is suggested this should be analyzed and discussed, other than this is a standard of care for patients over 70 years. Were all patients over 70 years osteoporotic? Is the only major parameter affecting patient outcomes the preexisting comorbidities, e.g. age as discussed? Hence the suggestion by this reviewer to have an explicit hypothesis, or hypotheses, that will guide the reader to the discussed conclusions and guide the authors to improved statistical analysis.

Reply 2: Thanks for your comments. One of the major concerns about surgery in elderly patients is that they usually have fragile bones, which means that instrumentation is associated with an increased complication rate. As we commented in the first paragraphs of the discussion, the good clinical results obtained by the elderly patients in this study are due to direct decompression of neural elements and immediate stabilization of the spine with the most appropriate instrumentation. The mere placement of cemented instrumentation is not directly responsible for the improvement, since it is the extensive decompression that is responsible for the clinical improvement. However, without adequate stabilization, extensive decompression would have led to an unstable

postoperative spine. Therefore, cemented instrumentation is in our opinion a necessary cooperator for a good postoperative result in case of bone fragility.

BMD, as measured by DEXA, does not represent the bone quality of the lumbar spine exactly, as it is a two-dimensional imaging technique and degenerative change in the vertebra or calcification of the soft tissues, including the adjacent vascular structures, may overestimate its true value. For this reason, we do not leave the decision to perform a cemented augmentation solely in the hands of the DEXA result. The age of the patient, the history of previous osteoporotic fractures, history of chronic diseases associated with bone fragility, of a history of chronic treatments associated to bone fragility, and finally, the intraoperative tactile feel resistance of the vertebral body to the pedicle probe, or suboptimal grip feel upon insertion of the fenestrated transpedicular screw, are all factors that help in the decision to carry out cement augmentation.

Table 3 should be revised to include pedicle screw characteristics between groups and a regression analysis done to verify no effect of cementing and fenestrated screws or the presence of osteoporosis. The reason for this is that while the authors provide a thorough explanation for the use of fenestrated screws, and discuss their use for osteoporotic patients, they do not connect how their data justifies the need for this surgical treatment. A large amount of the Discussion is focused on fenestrated cemented screws and osteoporosis but it appears that bone quality was not a parameter of interest in the statistical analysis. It would move this paper from one that is interesting to one that has true impact by connecting bone quality and surgical treatment to elderly patient outcomes. An expanded study with more significant statistical methodology is suggested in any future work.

Reply 3: Thank you very much for your interesting admonition. Regression analysis is a statistical process to understand how one variable depends on another variable. In this case, I understand that the reviewer suggests a regression analysis to assess how a patient's age affects their bone fragility, thus finding a relationship between the two variables (age and BMD measured by DEXA scan) and thus plan the use of cemented instrumentation. However, according to the literature, half of fragility fractures occur in women with normal BMD. This represents a significant percentage of false negatives, so the validity of BMD as the sole criterion in decision-making is relative and its use as a screening tool would be doubtful, especially considering that the increase in age is 7 times more important than the densitometric decrease. For this reason, we have not yet found a better parameter than the combination of the patient's age (objective preoperative data), combined with the suboptimal grip feel upon insertion of the transpedicular screw (subjective intraoperative parameter) to make the decision to carry out the augmentation. In addition, performing a regression analysis with all the patients in the study would have implied performing a DEXA scan in patients from the young group, which we have not performed. However, the observation about the regression analysis seems important enough to us to take up the challenge and incorporate it into our current studies.

Changes in the text: (Page 12: Lines 21-24) "...and the validity of BMD as the only criterion in decision-making is relative and its use as a screening tool would be doubtful, especially considering that the increase in age is 7 times more important than the densitometric decrease (37)"

(Page 21: Lines 19-21) 37. Kanis JA, Borgstrom F, De Laet C, Johansson H, Johnell O, Jonsson B, Oden A, Zethraeus N, Pflieger B, Khaltsev N. Assessment of fracture risk. *Osteoporos Int.* 2005 Jun;16(6):581-9.

Spelling Line 187 "months"

Reply 4: Thank you for the correction.

Reviewer B

The article is very concise and interesting. As I asked the authors.

1) What exactly do you define the tactile resistance while surgery to use PMMA? Do you have any objective decision-making while surgery if any?

Reply 1: Thanks for the question. The introduction of the pedicle probe allows us to appreciate the bone resistance, discriminate the hardness of the bone, the interpretation of its consistency and thus apply an insertion force proportional to the ease with which first the probe and then the screw penetrates the thickness of the cancellous bone of the vertebral body. This is a subjective measure of the surgeon. We do not use any objective measure to discriminate the resistance of the cancellous bone of the vertebral body than the surgeon's perception of the tactile resistance of the vertebral body to the screw insertion instruments.

Lee JH et al. determined, in 2012, the correlation between bone mineral density (BMD) and the magnitude of torque required to insert a pedicle screw in a group of osteoporotic patients, by attaching a connector specifically designed to fit into the head of the pedicle screw, to a digital measuring device. The positive correlation found by the authors between BMD and the maximum torque required to insert a pedicle screw suggests that pre-operative assessment of BMD may be useful in predicting the strength of fixation of a screw. (Lee JH, Lee J, Park JW, Shin YH. The insertional torque of a pedicle screw has a positive correlation with bone mineral density in posterior lumbar pedicle screw fixation. *J Bone Joint Surg Br.* 2012;94-B(1):93-97)

2) The percentage of the main cases of 2 Groups are quite different. degenerative disc disease vs. stenotic disease. What would you say the difference? I guess the difference would influence on the clinical results if compared the 2 Groups.

Two above in my concerns.

PS. Nowadays, PLIF is a main stream of the lumbar fusion surgery rather than PLF.

Reply 2: Thanks for your comments. The difference in diagnoses in both groups is the consequence of the prevalence of the disease based on the age of the patient. Lumbar stenosis is more prevalent in the elderly and degenerative disc disease is more prevalent in the younger adult.

Glassman et al, in 2008 reported the clinical outcome, stratified by diagnosis, among a series of patients with lumbar degenerative disease whose treatment included lumbar spine fusion. The mean age of patients with degenerative disc disease was nearly 20 years younger than the mean age of patients with spinal stenosis. The results of clinical improvement were very similar between both groups. The occurrence of major complications was more frequent in patients in the spinal stenosis group. These results of Glassman et al are very similar to those of our study.

Changes in the text: (Pages 15-16) "Glassman et al, reported the clinical outcome, stratified by diagnosis, among a series of patients with lumbar degenerative disease whose treatment included lumbar spine fusion. The mean age of patients diagnosed with stenosis was 63.3 ± 13.1 years, while the mean age of patients with degenerative disc disease was 46.7 ± 10.2 years. Assessment of the mean net change in ODI outcome score by diagnostic subgroup 1 year postoperatively revealed a substantial improvement for patients with disc pathology of 16.7 ± 16.0 points and for patients diagnosed with spinal stenosis, 16.1 ± 17.8 points at 1 year postoperatively. Assessment of the mean net change in back and leg pain outcome score by diagnostic subgroup 1 year postoperatively revealed an improvement for patients with disc pathology of 2.8 ± 2.9 and 2.0 ± 3.0 points respectively and patients diagnosed with spinal stenosis improved 3.1 ± 2.9 and 3.1 ± 3.2 points

respectively. The incidence of major complications was 8.7% in the stenosis subgroup and 3.0% in the disc pathology subgroup. The findings regarding clinical improvement and occurrence of complications are in line with the present study.”