Author's response to reviews

Title: Distribution of ossified spinal lesions in patients with severe ossification of the posterior longitudinal ligament and prediction of ossification at each segment based on the cervical OP index classification: A multicenter study (JOSL CT study)

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Reviewer reports:

(Reviewer 1): General Impression: Well-conducted, well-written, interesting study with pertinent and appropriate conclusions. Study pathology is important, especially in Asian countries.

Response: Thank you for your review of our paper.

I will comment on the article in order of each session:

Abstract:

line 197 - Consider the possibility of removing the word "cervical".
Although it seems obvious to those who already know the study, for those who start reading the Abstract, this phrase was confused. It may be more appropriate to use only the term "OPLL" (considering the whole column) instead of "cervical OPLL".

Response: As suggested, we have deleted the term in the Background section of the Abstract.

Statistics - I consider it necessary to include the reference of which regression method was used.

Response: We have added details about the method (a forward stepwise logistic regression model) in line 239 and added a reference (Ref# 7; Hicks GE et al. Arch Phys Med Rehabil 2005).

Results - Extensive data, however, well described.

Response: Thank you for the reviewing.

(Reviewer 2: Congratulations on the manuscript. I’ll comment and make my review according to each topic.

Response: Thank you for your review of our paper.

Abstract:

Please, add on the conclusion the main results (to answer the purpose of the study).
Response: We deleted the sentence in the previous version, and added the following sentences. “Thoracolumbar OPLL occurred most often at T1 in men and at T3/4 in women. In severe OPLL cases, although ossified lesions were frequently seen at the intervertebral and vertebral levels around the cervicothoracic and thoracolumbar junctions in men, OPLL could be observed more diffusely in the thoracic spine in women.” (Conclusion section of the abstract)

Introduction:

You used the word "however" in line 224 and 228. Please, replace one of them for another synonymous word.

Response: This has been replaced with “Nevertheless” (line 198).

Methods:

The WHO definition for adult is a person older than 19 years of age; for adolescent is a person who falls into the 10 to 19 years of age. What was the criteria for excluding people younger than 15 years of age?

Response: We defined the lower limit of age as 15 years because in our country, patients aged ≥ 15 years old are usually seen at the Department of Orthopedic Surgery; the youngest patient in the study was 30 years old. We agree with your suggestion and have changed the age of lower limit of age accordingly (line 210).

Patients who had undergone anterior decompression surgery for OPLL were excluded; and what about another cervical spine surgeries? Were them also excluded? (Did at least one patient had undergone another cervical surgery?).
Response: We excluded patients treated with anterior decompression for spinal compression because it is impossible to evaluate the precise distribution of OPLL in such cases. Indeed, 3 patients treated with posterior decompression surgery for thoracic OPLL were included. In these 3 cases, ossification was not removed in each case and CT scans were obtained immediately after the operation. There was no patient undergoing cervical spine surgery for compressive lesions. Because OPLL can be basically confirmed even in patients treated with posterior decompression surgery, we decided to include such patients.

Line 240: "Four hundred and fifty-six patients with OPLL were identified, of whom only 322 had full clinical, demographic, and anthropometric data available for analysis". How was this identification made? Was it a medical report revision of all the patients of the institution? Who made that? Were then called back after a medical report review to make the CT examination for the study or they also did it for another reason? And if there was a recall for the exam, were medical data collected again for study (symptoms and physical examination)? Please, clarify.

Response: First, we decided to accumulate patients diagnosed with cervical OPLL by plain X-rays who presented with either neck pain, numbness in the upper and/or lower extremities, clumsiness, or gait disturbance and who underwent whole spine CT. We requested 20 institutions to assign such patients to the study. Each institution assigned cervical OPLL patients in the registry format of the study. After gathering 456 samples to the central office of this multicenter study, we made a chart of data, combining OPLL distribution obtained by CT with basic data such as age, sex, presence of diabetes, and body mass index for each patient. In this step, absence of at least one aspect of basic or CT data was noted for many patients. Therefore, the central office requested the respective institutions to recall the patients and recollect as much basic data as possible. Nevertheless, missing data was noted for a total of 134 patients (missing basic data in 86 patients and incomplete CT data in 48 patients). We thus excluded these 134 samples. We have now added a flow chart for clarity (Figure 1).
The reason for excluding patients was only because of the available data or was it also for the other exclusion criteria you have written before? Please, clarify. A flow chart could be used for a better understanding of the patients' inclusion.

Response: As mentioned above, we excluded 134 patients because of missing data. There were no patients excluded based on exclusion criteria in this study. Therefore, we added Figure 1 for clarity.

You used many times the term incidence. The incidence of a disease is the rate at which new cases occur in a population during a specified period. And the prevalence of a disease is the proportion of a population that are cases at a point in time. You detected patients by medical reports and cervical radiographs and then, you made CT of total spine. Since there was only one evaluation of total spine, isn’t the term incidence incorrect? Please, explain and replace the terms incidence for prevalence if appropriated.

Response: We investigated the proportion of patients with a specific disease at a certain point. We thus replaced ‘incidence’ with ‘prevalence’ as suggested.

Why the study does not have a control group?

Response: At the National Society of the Study of Ossification of the Spinal Ligaments, we developed a case series for this study to retrospectively investigate predisposition to hyperostosis in patients with OPLL. Therefore, this is why the study does not have a control group. In addition to the case series, we started another prospective study comparing radiologic and clinical features between OPLL patients and patients with cervical spondylosis (control-arm patients) and we intend to analyze the differences.
Results

Again, you used the term incidence, instead of prevalence. Please, explain and replace the terms if appropriated.

Response: The term ‘prevalence’ is more suitable to explain the frequency of OPLL. We have replaced “incidence” with “prevalence” as suggested.

Line 303 - separate 12.0fold - 12.0 fold.

Response: We corrected this accordingly (line 273).

I suggest you put the numbers with the percentage in each data you have showed. For example, you could write in line 278: "... and 31.7% (102 / 322) of the patients had diabetes mellitus."

Response: We added the number of patients (lines 248 and 252) and percentages (lines 249-250).

Discussion

Line 341: "To the best of our knowledge, there has been no detailed research on the prevalence of OPLL at each spinal level or on the levels most likely to contain ossified lesions in patients with cervical OPLL". This sentence is not correct. The reference number 6 made that (on that study’s results, page 4, there is the "Prevalence of OPLL in the thoracolumbar spine in patients with cervical OPLL" and on the page 6 there is "The cervical OP-index classification for prediction of the presence of OPLL in the thoracolumbar spine"). So, you must exclude this sentence or rephrase it in another way.
Response: We understand what the referee meant. We have removed this sentence in the Discussion section.

Line 354: "This is the first multicenter study to review the distribution of ossification in patients with severe OPLL". This is also not correct, and the example is reference 6. So, you must exclude this sentence or rephrase it.

Response: We have also deleted this from the Discussion section.

Line 391: "...we could not evaluate clinical symptoms". But what about line 237: "... as well as symptoms, such as neck pain, numbness in the upper and/or lower extremities, and clumsiness or gait disturbance"? And line 241: "... of whom only 322 had full clinical, demographic, and anthropometric data available for analysis".

So, did you have access to those data, even in a retrospective way or not? And if you had, why did you decide not to use it? Please, clarify that.

Response: To clarify, we collected data of patients who presented with either symptoms of neck pain, numbness in the upper and/or lower extremities, clumsiness, or gait disturbance. However, the data did not include quantitative measurements of clinical symptoms (i.e. numeric rating scale, SF-36, neck disability index, Japanese versions etc.), and so we could not evaluate the severity of neurologic disorder in each patient. We added “quantitative measurements” (lines 358-9) and deleted the term “clinical” (line 231) to avoid confusion.