

Format for ANSWERING REVIEWERS

June 19, 2015

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name: 17581-review.doc).

Title: Volume and fat infiltration of spino-pelvic musculature in adults with spinal deformity

Author: Bertrand Moal, Nicolas Bronsard, José G. Raya, Jean Marc Vital, Frank Schwab, Wafa Skalli, Virginie Lafage.

Name of Journal: *World Journal of Orthopedics*

ESPS Manuscript NO: 17581

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Answer to the reviewer has been addressed as follow:

Reviewer 02444745

This is an article about volume and fat infiltration of spino-pelvic musculature in adults with spinal deformity. However, there are some problems. At first, a display of the spinal deformity of the subjects is nycterine, and the subjects might include variable deformities with variable parameters. There is no comparison between subjects and control. The relationship between volume and fat infiltration and spinal deformity is unclear.

Thank you for this comment. The results section includes a description of the spino-pelvic parameters (ie spinal deformity) in the coronal and sagittal planes. Those results illustrate the diversity of our population. As developed in the discussion section, the various deformities presented in this population limited the ability to associate changes in a specific muscle groups with a specific type of deformation. The fact that there is no control population has also been highlighted in the limitation section of our discussion.

However we believe that the methodology described in the article, the results on the inhomogeneous distribution of the fat infiltration, and the greater impact of muscle degeneration on spinal erector are important steps toward a better understanding of this pathology and deserve to be reported.

Reviewed by 02348457

Grade B (Very good) /Grade A: priority publishing / Accept

1. the sample size is small, as only 19 patients.

Thanks a lot for this comments, as explained in the discussion the small size number limits the impact of our study. In an effort to clarify this point, the following sentence has been as a limitation in the discussion:

" Due to our experimental design and the limited sample size, we cannot draw any definitive conclusions correlating ASD and muscular factors. "

However we believe that the methodology described in the article, the results on the inhomogeneous distribution of the fat infiltration, and the greater impact of muscle degeneration on spinal erector are important steps toward a better understanding of this pathology and deserve to be reported.

2. Why only female patients were included, male patients were excluded?

Only female patients were included because adult spinal deformity is a pathology affecting mainly female patients. Given our small sample size, the inclusion of male patients would have created an important confounding factor (ie due to the difference in female versus male muscular system). Therefore, our decision was to limit the enrollment to female patients only. The discussion was updated as follows:

"Given the fact that the prevalence of adult spinal deformity is greater in female than in male patients, only female subjects were included in this study in an effort to limit confounding factors related to gender's difference in muscular system. "

3. More Figures illustrating fat infiltration and muscle loss.

New figures were added to illustrate fat infiltration and muscle loss

Reviewed by 03069451

Grade A (Excellent) / Grade A: priority publishing / Accept

This manuscript presents a well-designed study with an accurate analysis of volume and fat infiltration of spino-pelvic-lower limb musculature in 19 patients with spinal deformity. The topic is original, interesting and useful for the orthopedic and rehabilitation community. The study is well performed and well described and, even if the sample size is not large, the accurate methods of analysis using MRI improve the value of the results. In my opinion the manuscript could be accept as is.

Thanks for these comments

Reviewed by 03067964

Grade D (Fair) /Grade B: minor language polishing /Major revision

This manuscript describes an observational study of volume loss and fat infiltration of muscles associated with sagittal posture in patients with adult spinal deformity. I have just a few comments on the methodology.

1. The study design is unclear with respect to analysis units and how patients contribute observations to the different comparisons. It is important to recognize that the used statistical methods require statistically independent observations, see e.g. Ranstam J. Repeated measurements, bilateral observations and pseudoreplicates, why does it matter? *Osteoarthritis Cartilage* 2012;20:473-475.

Thanks a lot for this comment. To our knowledge the analysis unit are respected because there is no repetition of measurement. Several muscles as Psoas are included in different muscular groups, however the muscular groups are analyzed separately.

2. It is also unclear whether other underlying assumptions (such as Gaussian distribution and homogeneous variance) are fulfilled and how this has been evaluated.

For Anova test, homogeneity of variance were performed and following the results, either Bonferonni or Games-Howell was used. In order to clarify this point, the method section has been updated as follows:

" For Anova test, homogeneity of variance were performed and following the results, either Bonferonni or Games-Howell was used ".

3. The purpose of investigating the relationship between muscle parameters and demographic data

is unclear and should be explained. Depending on the purpose of the statistical analysis may need to be revised. For example, if the authors wish to estimate risk factors for volume loss and fat integration, a multiple regression model including adjustment for potential confounding factors may be useful. The inclusion of covariates should then be carefully considered, see Schisterman EF, Cole SR, Platt RW. Overadjustment bias and unnecessary adjustment in epidemiological studies. *Epidemiol* 2009;20:488-495 and Cole SR, Platt RW, Schisterman EF, Haidao C, Westreich D, Richardson D, Poole C. Illustrating bias due to conditioning on a collider. *Int J Epidemiol* 2010;39:417-420.

Thanks you for this comment and both articles. The purpose of the statistical analysis was to evaluate the correlation between the muscle's groups parameters and age and BMI and not to evaluate the risk factors for volume loss and fat integration.

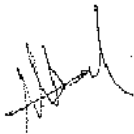
4. The purpose of hypothesis testing the phantom data should be described. What kind of variability is tested?

In order to obtain the fat infiltration inside each muscle, MRI acquisition with 2 points Dixon method were performed. The phantom were used to control the ability of this method to distinguish between fat and water. No variability was tested.

5. The presentation of results should include information on the inferential uncertainty of estimated parameters, preferably in terms of 95% confidence intervals.

Thanks you for this comments. The 95% confidence intervals have been add for the demographic data, the muscular volume, the percentage of Fat component and the Ratio Flex/Ext.

: corrected



manuscript in the *World Journal of Orthopedics*.

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