

## Peer review file

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### Reviewer A

The authors retrospectively studied the adjacent segment degeneration (ASD) related signs following a lumbar fusion procedure (263 patients).

Postoperative disc height loss was observed in 159 free discs among 112 patients (42.6%) (95% CI 36.4-48.8). Anterior or posterior slippage (anterolisthesis or retrolisthesis) at the end of the follow-up period was observed in 33 patients (12.5%). Upper segment rotation increased in the postoperative period in 36 patients (13.6%). Radiological disc degeneration was observed in 107 discs among 72 patients, being more frequent in the immediate upper disc with grade 2 and 3 changes at the end of follow-up in 48 discs from 35 patients (13.6%) (95% CI 13.4-23.1). Radiological adjacent segment degeneration signs were observed in 151 patients (57.4%; 95% CI: 51,2-63,6) and 53 of them (20.2%; 95% CI: 15.1-25.2) who also showed clinical adjacent segment degeneration symptoms (clinical and radiological adjacent segment degeneration). Degeneration changes with degrees IV and V shown by a preoperative and magnetic resonance (MR) study at end of the follow-up period performed in 73 patients (27.7%), were observed in 46 discs among 32 patients (43,8%) (95% CI 31.8-67 55.9).

Radiological ASD signs evaluated in every free disc following a lumbar fusion procedure are observed with a variable frequency. The authors concluded that the ASD was assessed with mechanisms of compensation of lordosis loss and should be taken into consideration in a prospective revision surgery.

This is an interesting report regarding lumbar foraminal stenosis. Before resubmitting the article, I request some major changes as follows.

Major point:

**Comment 1:** The most critical point is that the several different subjects were included in this study. For example, incidence of ASD might be different depending

on fusion type and the extent of fusion level. PL (the authors did not indicate this abbreviation in the text. Does this mean PLF [posterior lumbar fusion without instrument?]) can preserve small motion of the spine thereby the incidence of ASD is lower than that of PLIF/TLIF. Furthermore, long fusion occurs more higher incidence of ASD than single-level fusion (The authors shortly indicate this in Results section). I recommend to diffidently analyze the incidence of ASD according to the operative procedures. The reason why above-mentioned analysis is important is that we do not know the natural course of degeneration of spine. Some degeneration in this study might include natural spine degeneration, because the observation period in this study is sufficiently long (range 24 to 82 months, a mean of 45.9 months).

**Reply 1:**

**1.-This article is complementary to the one cited above: J. Ramirez-Villaescusa, J. López-Torres Hidalgo, A. Martin-Benlloch et al. "Risk factors related to adjacent segment degeneration: retrospective observational cohort study and survivorship analysis of adjacent unfused segments". Br J Neurosurg. 2019;33(1):17-24.**

**2.- It is a cohort study, and the variables fusion type and fusion levels were analyzed. This article is part of the work carried out to determine the survival of free discs. To asses risk factors of ASD, the following variables were analyzed: diagnosis, type of instrumentation (lateral connector screws vs. superior loading screws), type of fusion (posterolateral vs. circumferential), instrumented levels (one vs. two or more), postoperative lordosis (normo- or hypolordosis vs. postoperative hyperlordosis). The results showed that both multilevel fusion and the use of superior loading screws were variables associated with ASD.**

**CHANGES IN THE TEXT:**

**The abbreviation PLF (posterolateral fusion) is now indicated in section material and methods line 77.**

**Comment 2:** The most interesting point of this study is the discrepancy between radiological ASD and clinical ASD (apparent symptoms by ASD). The authors described as follows: 53 patients were considered as symptomatic (clinical ASD) and

98 patients (37.4%) with radiological changes did not present symptoms. Lumbar or radicular pain only persisted in 19 patients (7.2%), not shown radiological changes 93 patients (35.4%) presented no clinical or radiological changes (Table 4). It seems better to analyze the predictive factors of this discrepancy from radiological findings for the readers of JSS.

**Reply 2:**

**1.- Most studies report the appearance of radiological signs during follow-up but only in a small percentage do these changes cause pain or disability requiring a second procedure.**

**2.- Radiological changes (listhesis, rotation, loss of disc height, radiological disc degeneration and disc degeneration on MRI) considered as ASD were more frequent in the first disc superior to the fused disc (21.3%), in the second superior disc (18.6%) and in the inferior disc (17.1%).**

**3.- The number of signs was more frequent in a single disc (20.9% in the superior disc, 19.8% in the second disc, 16% in the third disc, 3.8% in the fourth disc and 11.4% in the inferior disc).**

<b>N° Changes disc</b>	<b>1st upper disc</b>	<b>2nd upper disc</b>	<b>3rd upper disc</b>	<b>4° upper disc</b>	<b>below disc</b>
1	55(20.9%)	52(19.8%)	42(16.0%)	10(3.8%)	30(11.4%)
2	21(8.0%)	17(6.5%)	10(3.8%)	1(0.4%)	10(3.8%)
3	24(9.1%)	12(4.6%)	5(1.9%)	2(0.8%)	5(1.9)
4	7(2.7%)	4(1.5%)	3(1.1%)	-	-
5	1(0.4%)	-	-	-	-

Number of x-ray changes

**Comment 3:** The conclusion “All free discs after fusion were assessed as they could indicate mechanisms of compensation of lordosis loss” is overly estimated. Because the authors did not calculate exact lordosis angle or previously known lordosis parameters.

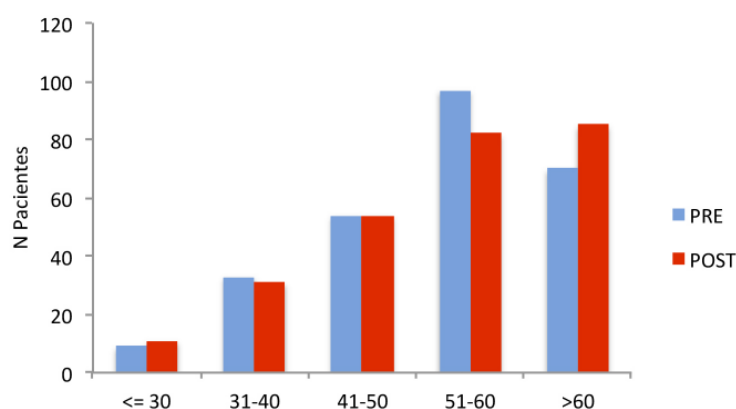
**Reply 3:**

**1.- L1-S1 lumbar lordosis (LL) decreased in patients with preoperative LL of 51-60°, increased postoperatively in patients with preoperative lordosis of >60° and remained unchanged in patient with preoperative lordosis of 30-50°.**

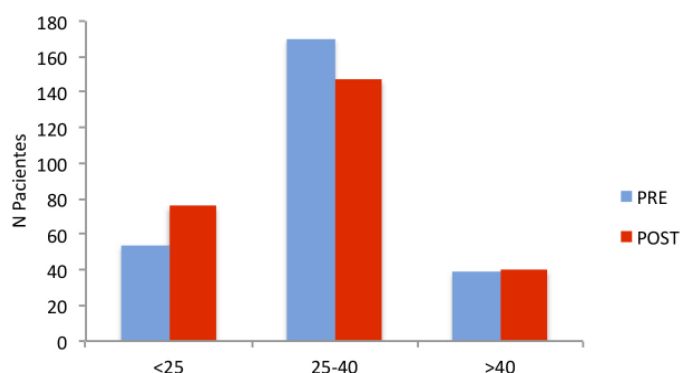
**2.- L4-S1 lumbosacral lordosis (LSL) decreased in patient with preoperative LLS of 25-40°, increased postoperatively in patients with preoperative LLS of <25°, and remained unchanged postoperatively in patients with preoperative LLS >40°.**

**CHANGES IN TEXT:**

**This comment is now added in pag 10 line 150-155**



Lordosis lumbar total (L1-S1)



## Lordosis lumbosacra (L4-S1) lumbosacral (LSL)

### **Reviewer B**

In their manuscript, “A DESCRIPTIVE STUDY ON THE ADJACENT SEGMENT DEGENERATION RELATED SIGNS FOLLOWING A LUMBAR FUSION PROCEDURE,” the authors perform a retrospective analysis to report on adjacent segment degeneration in patients undergoing lumbar fusion for degeneration/instability. To do so, they look at radiographic and clinical outcomes to grade disc degeneration based on the Weiner and Pfirrmann scores, rotation based on Nash-Moe grade, and degree of postoperative listhesis, as well as clinical symptoms.

While the authors should be commended for all of their hard work to study these patients, the manuscript suffers from multiple drawbacks. The major limitation of this study is its heterogeneous nature. The inclusion of all different types of pathologies (including both degen/isthmic spondy, lumbar stenosis, etc) as well as a broad range of surgeries including one to 4 level fusion and ranging from posterolateral alone to interbody fusion. Additionally, the broad range of follow-up time from 24 to 82 months is important in a study assessing adjacent level degeneration – a patient with 2 years of follow-up cannot be grouped together with a patient with 82 months, who may be expected to have more degeneration based on the substantial time that has passed since the index operation. Finally, the manuscript writing and organization could be significantly improved for clarity. There are grammatical, punctuation, and syntactic errors which should be addressed, and the ideas presented in the introduction and discussion could be much better organized for clarity.

Here are comments specific to each section:

Abstract

- The authors do not include a background on the topic. Instead they have a line describing the aim of their study.

**Reply:**

**CHANGES IN THE TEXT:**

The following sentence is now added lines 6 to 9“**Adjacent segment degeneration (ASD) is a frequent complication following vertebral fusion procedures and is defined as the condition where patients recover after the initial procedure but develop compatible symptoms with radiological injuries in the segments adjacent to the fused ones at a later stage**”.

In pag 6 Lines 63-65: **The objective of the study was to describe the frequency and to assess the radiological and clinical changes of adjacent segment degeneration related signs following a lumbar fusion procedure.**

- In methods/results the authors should describe demographics (age, gender, etc) as well as surgical details (no. of patients having posterolateral vs circumferential fusion).

**Reply:**

**Methods: 1) Demographics (age, gender)**

**Results: There were 98 men (37.3%) and 165 women (62.7%) with a mean age of 59.0 years (CI 95%: 57.6-60.5).**

**The PLF technique was used in 65.8% of the cases and TLIF/PLIF fusion technique in 34.2% of the cases**

**Table 1 is now added with demographics data.**

- Need to describe what type of circumferential fusion -> were these interbodies placed posteriorly or anterior/lateral?

**Reply:**

**As indicated in the Material and Methods section, the circumferential fusion technique was performed through a posterior approach via PLIF/TLIF with placement of autologous bone obtained from the surgical field and posterosuperior iliac spine and using cages of polyether ether ketone (PEEK) implant.**

- What is follow-up period and what % achieved that length of follow-up?

**Reply:**

**CHANGES IN THE TEXT:**

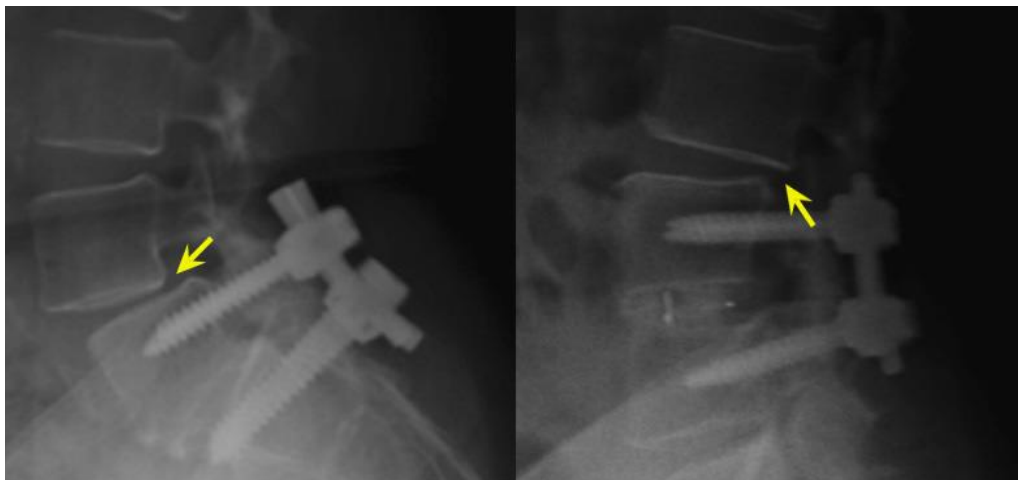
**The follow-up period ranged from 24 to 82 months, with a mean duration of 45.9 months (SD: 17.8) and a median of 43 months.**

**Added I the second paragraph of results line 137 and 138.**

- The authors report on % with listhesis but do not describe preoperative portion of listhesis.

**Reply:**

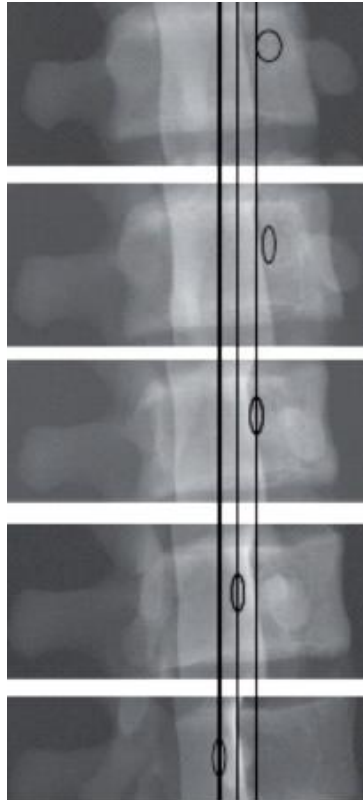
**Listhesis was considered as a criterion of degeneration when slippage of  $\geq 3$ mm was observed in the radiological study performed at the end of follow-up. In these cases, no listhesis was observed in the segment above or below the fused segment.**



-Same with rotational instability.

**Reply:**

**In the radiological study performed at the end of follow-up, any degree of rotation in the upper level to the fused one not present preoperatively, was considered as a sign of degeneration following Nash-Moe scale).**



- What grading scheme was used to grade the disc degeneration? Need to describe

**Reply:**

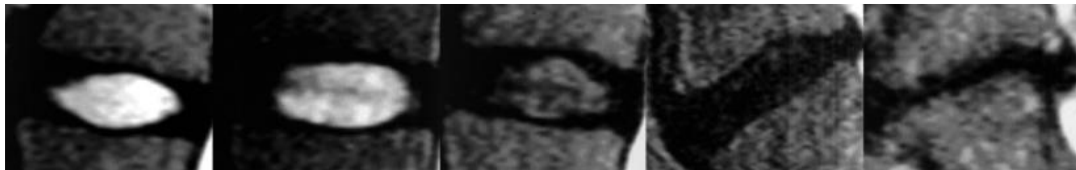
**Two scales were used:**

- 1) Radiological Weiner scale disk degeneration (0=normal, Grade 1= mild, Grade 2=Moderate and Grade 3= severe)**





**2) Magnetic resonance (MR) Pffirrmann scale degenerative disk disease)**



- Is “radiological disc degeneration” describing the operative level disc? Need to clarify.

**Reply:** The radiological classification according to the Weiner scale was evaluated in all lumbar free discs at the upper and lower levels in the preoperative and postoperative study, and in 72 patients underwent evaluation by magnetic resonance imaging according to Pffirrmann scale.

- The authors describe ASD postop but not preoperatively.

**Reply:** All signs considered as ASD were evaluated preoperatively and postoperatively at the end of follow-up.

**Pre- and postoperative degenerative disc changes are shown in Figure 4.**

- What are “clinical ASD symptoms”? Authors need to describe

**Reply:**

**The symptoms to define clinical ASD were the recurrence of low back and/or radicular pain assessed by visual analog scale (VAS), as well as the worsening of the degree of disability assessed by the Oswestry Disability Index (ODI).**

- The conclusions that ASD are observed with “variable frequency” is quite vague and does not add to our understanding of this topic

**Reply:**

**The incidence of adjacent segment degeneration is variable after a lumbar or lumbosacral fusion procedure and varies widely in the literature since the first descriptions in 1980.**

**The true incidence is difficult to define, since most studies are retrospective, with variable follow-up periods and dependent on the definition applied.**

**This paragraph is now added to the beginning of the discussion (page 11 lines 185 and 186)**

Background

- Need to understand what is novel about this study – what question are the authors trying to answer that we don’t already understand?

**Reply:**

**Most studies focus on the appearance of radiological changes in the adjacent segment immediately above or below that are related to the recurrence of low back and/or radicular pain. In this study all discs have been analyzed, which makes it possible to evaluate the changes in all the non-fused mobile segments that may be responsible for the symptoms. Focusing the analysis exclusively on the disc immediately above or below constitutes one of the main limitations of many studies when describing the true incidence of ASD.**

Methods

- How many levels did they limit inclusion criteria to? Which levels?

**Reply:**

**Patients with lumbar segmental fusion were included in which at least one free lumbar disc remained. Thus, patients with one-segment (L4-L5/L5-S1), two-segment (L3-L5/L4-S1), three-segment (L3-S1/L2-L5) and four-segment (L1-L5/L2-S1) fusions were included.**

- Very heterogeneous population – includes degenerative spondylolisthesis, isthmic spondylolisthesis, central stenosis, etc

**Reply:**

**The sample included is heterogeneous according to diagnosis, although the same PL or TLIF fusion technique was used.**

- What is follow-up period? Was there any minimum?

**Reply:**

**The follow-up period ranged from 24 and 82 months with a mean of 45.9 (SD: 17.8) and a median of 43 months**

- Skeptical that you can reliably measure 1 deg of rotational difference and the clinical significance of that

**Reply:**

**Any change of rotational deformity  $\geq 1$  degree in the upper level to the fused one following Nash-Moe scale was considered as a sign of degeneration.**

Results

- Very wide range of follow-up – difficult to compare patients at 24 months vs 82 months

**Reply:**

**The observation period ranged from 24 to 82 months, with a mean duration of 45.9 months (SD: 17.8) and a median of 43 months.**

**Due to the different observation period of the patients, we performed a survival analysis in the article referenced above (J. Ramirez-Villaescusa, J. López-Torres Hidalgo, A. Martín-Benlloch et al. "Risk factors related to adjacent segment degeneration: retrospective observational cohort study and survivorship analysis of adjacent unfused segments". Br J Neurosurg. 2019;33(1):17-24)**

- Why were patients with lumbar canal stenosis getting fusion?

**Reply:**

**The need for fusion in patients with canal stenosis is controversial in the absence of preoperative instability. Patients with canal stenosis and isolated decompression were excluded from the study. But sometimes wide decompressions with complete uni or bilateral medial facetectomy or associated with pars interarticularis lesion may require fusion to avoid postoperative instability.**

- Included patients with 1 to 4 level fusion – very heterogeneous and different amounts of stress placed on a disc depending on number of fused levels below  
**The variable "number of segments" was included in the survival analysis to establish the risk of the appearance of signs compatible with DSA.**

**Multisegmental fusion was associated with a higher risk of degeneration compared to short fusions of one or two segments.**

- With listhesis – need to report on preop % with listhesis, otherwise these data are not useful

**Reply:**

**A listhesis was considered when postoperative anterior or posterior slippage (anterolisthesis or retrolisthesis) was found in any free segment that did not exist preoperatively.**

- Clinical ASD – how were these symptoms correlated specifically with ASD level vs. having pain from the index level?

**Reply**

**Clinical and radiological DSA was considered when lumbar pain, lower limb pain or disability reappeared associated with any radiological change in any free segment adjacent to the fused segment**

- Report on risk of a second procedure but no statistics reported

**Reply**

**Table 4 shows the % of patients with no changes, those with only radiological changes, those with only clinical changes without radiological changes, those with only clinical changes and those with clinical and radiological changes that required a new procedure (53 patients). This number of cases represents 20.2%, with a 95% CI of 15.1 to 25.2, which has been added in the results section.**

- Figure 1 – need to compare with preoperative images so it is clear that ASD occurred (vs. these changes were present prior to surgery)

**Reply: ADS was considered when any of the signs mentioned above appeared in the segment above the fused segment, such as listhesis, rotation, loss of disc height and degenerative disc changes that did not exist in the preoperative study.**

**Reviewer C**

In this manuscript titled “A descriptive study on the adjacent segment degeneration related signs following a lumbar fusion procedure”, the authors presented a retrospective observation of 293 patients that aims to evaluate for the prevalence of adjacent segment degeneration (ASD) in multiple lumbar segments rather than just in the upper segments as is traditional in the literature. To the best of my knowledge, this was the most prominent justification for this study.

**Major Suggestions:**

Authors mention multiple measuring systems to measure disc height loss e.g. by Ekman et al. and Frobin et al. I would be curious to know whether there was a particular reason as to why the Farfan method was employed over these. Was this an arbitrary decision or was this based on a comparative study of different disc height measuring methods? In general, it would be important to elucidate the rationale for selecting one particular mode of evaluation over another.

**Reply:**

- 1.- The digital measurement system of our hospital was used and proved to be reliable in angular and linear measurements (Radiological Archive Images Measurements RAIM-PC).**
- 2.- Farfan and Ekman's methods allows a measurement of anterior, middle and posterior height and their comparison in pre- and postoperative study. Each free disc was reliably measured according to the described methods.**
- 3.- The choice of measurement method was based on individual preference and ease of implementation. In our study, similar to Ekman's study for digital disc height measurement shows a substantial of intra- and inter-observer reliability.**

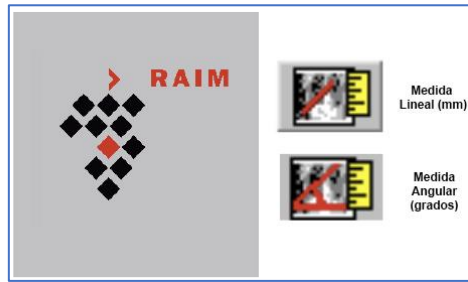
**CHANGES IN THE TEXT:**

**A comment about this is now added in pag 14 line 248-251**

Furthermore, considering that there is a complete lack of standing X-rays utilised in this study when the authors explains how sagittal/coronal balance, disc height loss etc. may be unnoticed in the supine position, it is crucial to support the validity of this study with a discussion on whether the aforementioned parameters can be properly evaluated in the supine position.

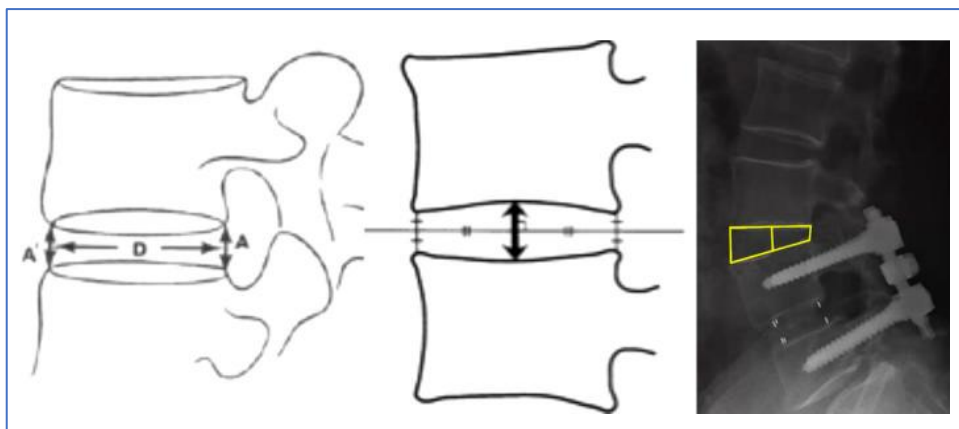
**Reply:**

- 1.- The preoperative and postoperative radiological study of the spine was performed in standing position, but only included the lumbosacral spine, so it was not possible to measure the spinopelvic parameters (pelvic incidence (PI), sacral slope (SS) and pelvic scale (PT)).**
- 2.-Angular measurements were taken in degrees and linear measurements in millimeters.**
- 3.- The computerized device for radiological measurement available in our hospital RAIM-PC (Radiological Archive and Images Measurement) was used.**
- 4.- The validity of the measurements was checked.**

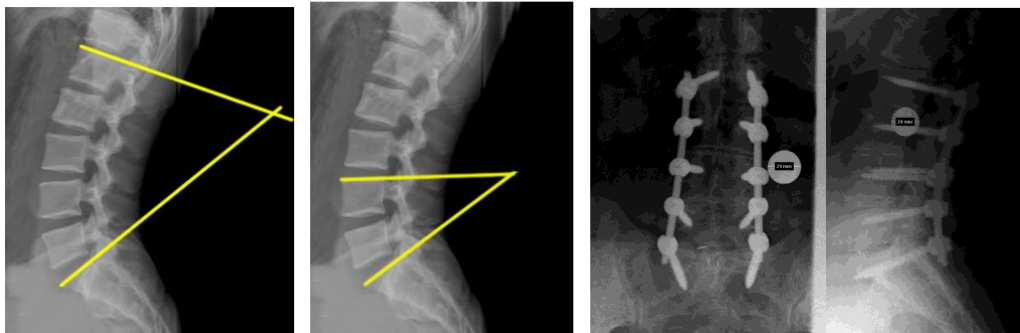


**Tube film distance**

**Radiological archive images measurement  
(lineal-millimeters and angle-degree)**



**Disc height measurement (Farfan and Ekmann methods of disk height measure)**



**Lordosis lumbar (LL) and lumbosacral lordosis (LSL) following Cobb method.**

Minor Suggestions:

It would be helpful to the readers to include a table to summarise the descriptive results regarding the patient demographics. These tables (table 1 and 2) were referenced but were not provided in the submission file.

**Reply:**

**Tables 1 and 2 are now provide, added and sent.**

There is significant amount of overlap in the results section. Of particular concern is the subsection 2- ASD criteria. Many of the results reported here were repetitions of the previous subsection 1- descriptive results.

**Reply:**

**Repeated results in the descriptive and ASD criteria subsection have been removed and are referred for display in Table 3.**

It was unclear how the authors recruited or selected the sample population. More information regarding the hospital/clinic the patients were recruited from, the number of surgeons that operated on the 293 patients and so on would be beneficial in determining significant sampling biases.

**Reply:**

- 1.- The sources of information for the study were the patient's clinical history and the radiology image archive of our hospital.**
- 2.- Demographic and preoperative clinical data, results of complementary examinations and diagnosis of the lesions were obtained from the clinical history.**
- 3.- Surgical protocol sheets were used to collect data on surgical techniques, fusion levels and types of devices used.**
- 4.- All interventions were performed by the same two surgeons with the lead surgeon being the first author of this study.**
- 5.- The patients were contacted by telephone and a clinical evaluation was made (neurological status and presence of lumbar and radicular pain) using VAS and ODI scales.**
- 6.- During the visit, after informing the patients of the nature of the study and obtaining their consent to participate in it, a radiological study was carried out.**

**CHANGES IN THE TEXT:**

**These comments are now added in the manuscript pag 7 line 81-87**



Line 89 of page 3: add “in” and “of” to the sentence “change [in] appearance [of] segments adjacent...”. Overall, it would be helpful to readers to clarify this sentence to explain the multifactorial origins of ASD.

**Reply:**

**CHANGES IN THE TEXT:**

**1.- “The change in appearance of segments adjacent” is now added in bold.**

Line 44 of page 5: This paragraph is also repeated in subsection 5: statistical analysis of your methods section.

**Reviewer D**

An interesting paper but with the fundamental flaw of a lack of control group. There is also lack of description of the pre and post-operative segmental lordosis across the fused segments which will influence the relative rate of deterioration of adjacent segments as well as any lumbopelvic parameters such as pre-op pelvic incidence and global lordosis mismatch. I'm afraid I don't feel this paper adds to the established literature for this subject.

**Reply:**

**1.- This is a follow-up study of a cohort of patients who underwent lumbar fusion surgery, aimed at describing the appearance of signs related to DSA.**

**2.- Pre and postoperative lumbar lordosis was measured in the radiological study of the lumbosacral spine standing radiography (Reply reviewer A). Significant differences were found in the risk of degeneration (comparative analysis of lordosis) hypolordosis vs normo or hyperlordosis). Postoperative hypolordosis was significantly higher risk than normo or hyperlordosis in bivariate analysis but not in Cox proportional hazards analysis.**

**CHANGES IN TEXT:**

**This comment of pre and postoperative lumbar lordosis is now added in pag 10 line 150-155.**

**3.- The absence of radiographs of the complete spine in standing position did not**

allow an analysis of parameters related to sagittal deformity such as pelvic incidence (PI), sacral slope (SS) and pelvic scale.

