



Biomechanical analysis of laminectomy, laminoplasty, posterior decompression with instrumented fusion, and anterior decompression with fusion for the kyphotic cervical spine

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Abstract

Purpose Anterior and posterior decompressions for cervical myelopathy and radiculopathy may lead to clinical improvements. However, patients with kyphotic cervical alignment have sometimes shown poor clinical outcomes with posterior decompression. There is a lack on report of mechanical analysis of the decompression procedures for kyphotic cervical alignment.

Methods This study employed a three-dimensional finite element (FE) model of the cervical spine (C2–C7) with the pre-operative kyphotic alignment (Pre-OK) model and compared the biomechanical parameters (range of motion (ROM), annular stresses, nucleus stresses, and facet contact forces) for four decompression procedures at two levels (C3–C5); laminectomy (LN), laminoplasty (LP), posterior decompression with fusion (PDF), and anterior decompression with fusion (ADF). Pure moment with compressive follower load was applied to these models.

Results PDF and ADF models' global ROM were 40% at C2–C7 less than the Pre-OK, LN, and LP models. The annular and nucleus stresses decreased more than 10% at the surgery levels for ADF, and PDF, compared to the Pre-OK, LN, and LP models. However, the annular stresses at the adjacent cranial level (C2–C3) of ADF were 20% higher. The nucleus stresses of the caudal adjacent level (C5–C6) of PDF were 20% higher, compared to other models. The PDF and ADF models showed a less than 70% decrease in the facet forces at the surgery levels, compared to the Pre-OK, LN, and LP models.

Conclusion The study concluded that posterior decompression, such as LN or LP, increases ROM, disc stress, and facet force and thus can lead to instability. Although there is the risk of adjacent segment disease (ASD), PDF and ADF can stabilize the cervical spine even for kyphotic alignments.

Keywords Finite element method · Alignment · Laminoplasty · Laminectomy · Posterior decompression with instrument fusion · Anterior decompression with fusion · Kyphosis · Adjacent segmental disease

Introduction

Cervical decompression procedures are required for patients with symptoms such as cervical spondylotic myelopathy

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(CSM) and cervical ossification of the posterior longitudinal ligament (C-OPLL) [1]. These procedures have been reported to have good clinical outcomes [2, 3], but recently there have been reports of poor clinical outcomes for posterior decompression, depending on the preoperative cervical alignment [2, 4]. Especially in patients with a kyphotic cervical alignment, there have been multiple reports of postoperative complications such as instability and axial pain [4]. To deal with these complications, there are reports that suggest anterior or posterior decompression and fusion can be effective even in kyphotic cervical alignment cases [5, 6], though surgeons often use the technique that they are most familiar with. This comparative study of the biomechanical changes after decompression procedures may aid surgeons in pre-operative surgical planning. No reports in published literature have examined the biomechanical changes for patients with the pre-operative kyphotic cervical spine for different decompression procedures. We hypothesize that the anterior and posterior decompression with fusion may provide better stability than laminectomy or laminoplasty but stresses in spinal column may be higher compared to other surgical procedures.

In this study, a C2-C7 three-dimension finite element (3D-FE) kyphotic cervical spine model was utilized to examine how stresses and mobility change in the cervical spine for four decompression procedures: laminectomy (LN), laminoplasty (LP), posterior decompression with instrument fusion (lateral mass screw) (PDF), and anterior decompression with fusion (ADF).

Material and methods

Model development

A 3D FE model of the cervical spine (C2-C7) was created based on the computed tomography (CT) images of an adult male subject. Necessary approvals for use of these images were obtained from the institutional review board and ethics committee at the corresponding author's institution. The model was created using MIMICS (Materialise, Leuven, Belgium). The geometry of tissues was meshed with hexahedral elements using the IA-FE MESH software (IA, United States). The mesh convergence study was undertaken for the model. The seed size for the mesh was gradually decreased (3 mm, 2 mm, 1 mm, and 0.5 mm). The deviation in the results was less than 5% for the mesh size of 0.5 mm and 1 mm. Therefore, finer mesh size was not used as that would have added computational cost with a negligible difference in the results. Thus, the mesh size between 0.5 mm and 1 mm was considered optimal for our study [7]. We used the ABAQUS software (Dassault Systèmes, Simulia Inc., Providence, RI, USA) for FE analysis. The anterior

longitudinal ligament (ALL), posterior longitudinal ligament (PLL), interspinous ligament (ISL), supraspinous ligament (SSL), capsular ligament (CL), and ligamentum flavum (LF) were added as truss elements. The outer layer of the vertebrae represented a cortical shell, and the inside represented a cancellous bone. The intervertebral discs contained the annulus fibrosus and nucleus pulposus. The annulus consisted of a ground substance and embedded fibers oriented at $\pm 25^\circ$ [8]. The facet joints in the current model were represented using the surface-surface sliding contact, whereas the Lushka's joints in the lower cervical intervertebral discs were modeled using GAPUNI elements [9]. The material properties for all the structures in the FE model were taken from the literature (Table 1) [9–14]. The model validation was undertaken for the normal lordotic cervical spine FE model by comparing the range of motion (ROM), intradiscal pressure, and facet contact forces with the published in-vitro data in our previous study [15] (Fig. 1A). This model was the validated lordotic cervical spine with no surgical intervention. The validated lordotic cervical spine with no surgical intervention was then modified to represent the kyphotic cervical alignment.

Development of kyphotic cervical alignment model

Cervical spine alignment parameters reported in the literature were used to develop a kyphotic model [16]. The following parameters were modified in the C2-C7 model: cervical sagittal vertical axis (cSVA): the distance from a vertical plumb line dropped from the center of the C2 vertebral body to the posterior superior corner C7 vertebra, C7 slope: the angle between a horizontal reference line and a line parallel to the upper endplate of C7 and cervical kyphosis: the angle between the inferior endplate of C2 and the inferior endplate of C7 in the lateral view [17]. The validated lordotic cervical spine with no surgical intervention had following parameters—C2-C7 kyphosis angle: -5° , cSVA: 25 mm, the C7 slope: 22° .

We created the pre-operative kyphotic (Pre-OK) model by using the validated lordotic cervical spine with no surgical intervention. The C7 vertebrae were fixed, and pure moment was applied at C2 such that uniform load is transferred through all the vertebrae. The pure moment was applied until the desired C2-C7 cobb angle was achieved. The cervical spine sagittal parameters were iteratively modified to develop the Pre-OK model leading to C2-C7 kyphosis angle: 10° , cSVA: 38 mm, the C7 slope: 24° (Fig. 1 C, D). However, no validation was done for the pre-operative kyphotic cervical spine model due to lack of available in-vitro data for kyphotic cervical spine.

Table 1 Material properties assigned to the finite element model [9–14]

Component	Material properties	Constitute relation	Element type	Area (mm ²)
<i>Bone</i>				
Vertebral cortical bone	$E = 10,000 \text{ MPa}$ $\nu = 0.3$	Isotropic, Elastic	C3D8	–
Vertebral cancellous bone	$E = 450 \text{ MPa}$ $\nu = 0.25$	Isotropic, Elastic	C3D8	–
Vertebrae-posterior	$E = 3500 \text{ MPa}$ $\nu = 0.25$	Isotropic, Elastic	C3D10	–
Artificial bone	$E = 10,000 \text{ MPa}$ $\nu = 0.3$	Isotropic, Elastic	C3D8	–
<i>Intervertebral disc</i>				
Ground substance of annulus fibrosis	$C10 = 0.7$ $C01 = 0.2$	Hyper-elastic, Mooney-Rivlin	C3D8	–
Nucleus pulposus	$C10 = 0.12$ $C01 = 0.03$ $D1 = 0$	Incompressible Hyper-elastic, Mooney-Rivlin	C3D8	–
<i>Ligaments</i>				
Anterior longitudinal Ligament	15.0(< 12%), 30.0(> 12%) $\nu = 0.3$	Non-linear, Hypoelastic	T3D2	6.1
Posterior longitudinal Ligament	10.0(< 12%), 20.0(> 12%) $\nu = 0.3$	Non-linear, Hypoelastic	T3D2	5.4
Capsular ligament	7.0(< 30%), 30(> 12%) $\nu = 0.3$	Non-linear, Hypoelastic	T3D2	46.6
Ligamentum Flavum	5.0(< 25%), 10.0(> 25%) $\nu = 0.3$	Non-linear, Hypoelastic	T3D2	50.1
Interspinous Ligament	4.0(20–40%), 8.0(> 40%) $\nu = 0.3$	Non-linear, Hypoelastic	T3D2	13.1
<i>Facet joints</i>				
Apophyseal Joints	Non-linear Soft contact, GAPPUNI elements	–	–	–
<i>Lateral mass screw</i>				
Ti-Alloy	$E = 110,000 \text{ MPa}$ $\nu = 0.3$	Isotropic, Elastic	C3D4	–

Development of laminectomy (LN) model

To simulate laminectomy at a cervical spine level, ISL and SSL were resected. Part of the lamina elements was removed until the medial side of the facet joints. This method was used to create laminectomies at C3–C5 levels (LN model) (Fig. 2A).

Development of laminoplasty (LP) model

The double-door laminoplasty was simulated by first resecting the ISL and SSL. Following that, the spinous process was

partially resected, and the mesh of center of the lamina was deleted [18]. The mesh of medial side of both the facet joints was partially deleted so that lamina could be opened. The C2–C3 and C5–C6 LF were removed to open the lamina to the lateral side from the center. The graft was set with a height of 6 mm and a width of 8 mm, with the length adjusted to fit each opened lamina (Fig. 2B). The material properties of the bone graft were the same as the cortical bone. The bone graft was connected to the lamina using the “TIE” constraint in Abaqus software. Laminoplasty was created at the C3–C5 (LP model) (Fig. 2B).

Fig. 1 Creation of kyphotic alignment from the validated lordotic cervical spine with no surgical intervention. **A** the validated lordotic cervical spine with no surgical intervention: pure moment applied to C2 until C2-C7 Cobb angle of 0° was achieved. **B** Straight Alignment: pure moment applied to C2 until C2-C7 Cobb angle of -10° was achieved. **C, D** the pre-operative kyphotic (Pre-OK) finite element (FE) model

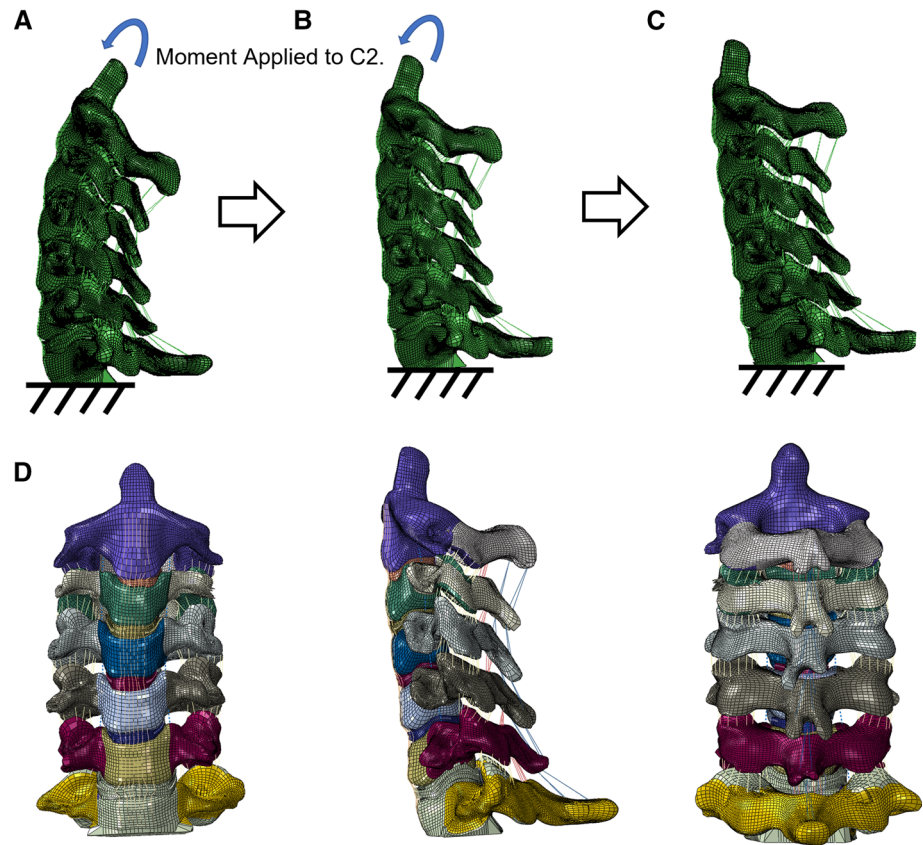
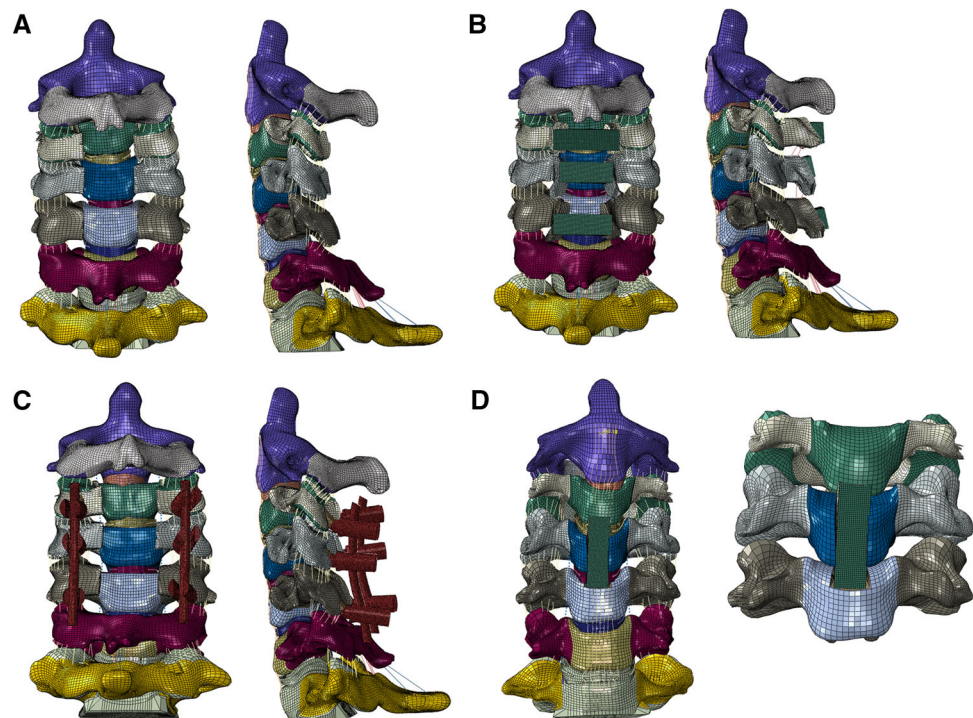


Fig. 2 **A** The C3-C5 laminectomy (LN) model. **B** The C3-C5 laminoplasty (LP) model. **C** The C3-C5 posterior decompression fusion (PDF) model. **D** The C3-C5 anterior decompression with fusion (ADF) model



Development of the posterior decompression with instrumented fusion (PDF) model

The LN models were used as a baseline for the creation of the PDF models. The instrumentation in those models comprised of 3.5 mm diameter and 16 mm length C3, C4, and C5 lateral masses screws (LMS). Next, a 3.5 mm rod was connected to the head of the lateral mass screws. The lateral mass screws and rods were assigned titanium alloy (Ti-Alloy) material properties [19]. The interaction between the screw head-rod was simulated via “TIE” constraint in Abaqus software to simulate rigid connection between these components. A screw-bush and bush-bone interface was utilized to simulate the pedicle screw fixation. For the screw-bush interface, the “TIE” constraint was defined between the outer surface of the screw and the inner surface of the bush. Next, the bush-bone interface was simulated by using the “Coupling” constraint. This method was used to create PDF at the C3–C5 levels (PDF model) (Fig. 2C).

Development of the anterior decompression with fusion (ADF) model

This surgical technique was simulated by removing the ALL, PLL, anterior portion of the annulus, and complete nucleus at the operated level (C3–C5). In ADF, the caudal endplate of C3 and the cranial endplate of C5 were trimmed. The cranial endplate, caudal endplate, middle cortical bone, and cancellous bone of C4 were also trimmed. Assuming that the bones were taken from the ilium, trimmed rectangular graft bone was placed in the trimmed space. The grafted bone was connected to the decompressed area of the vertebral body using the “TIE” constraint in Abaqus software. This method was used to create ADF at the C3–C5 levels (ADF model) (Fig. 2D) [20].

Loads and boundary conditions

The inferior endplate of the C7 was fixed under all motions. The model was subjected to the compressive follower load of 100 N with a pure moment of 1.5 Nm to represent the weight of the head/cranium and cervical muscle stabilization [21] and simulated flexion/extension, left/right lateral bending, and left/right axial rotations [11].

Data analyses

The intersegmental ROM, the global ROM, annulus stresses, intradiscal nucleus stresses, and facet contact forces were calculated for the Pre-OK, LN, LP, PDF, and ADF models. The global ROM means the relative ROM between C2–C7. Thus, global ROM (C2–C7 ROM) is the ROM of the entire cervical spine. Annular stresses and nucleus stresses were

noted by recording the maximum von Mises stress value. For the facet joint force, the data were averaged for the right/left lateral bending and axial rotations. The percentage change (%) was calculated using the following equation:

Percentage change (%)

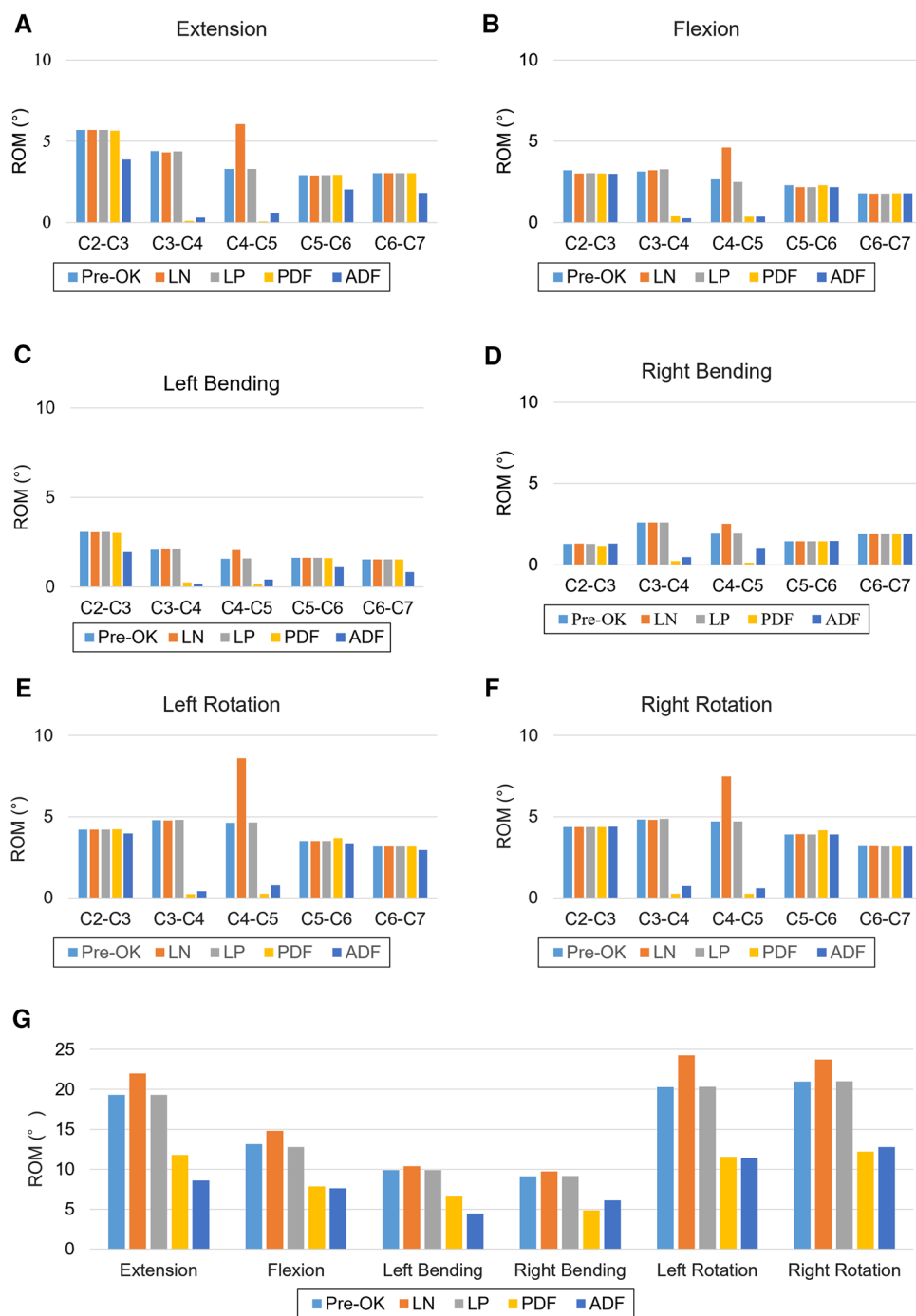
$$= \frac{\text{Operation model}_{\text{Data}} - \text{Pre-OK}_{\text{Data}}}{\text{Pre-OK}_{\text{Data}}} \times 100$$

Results

ROM

An increase in the global ROM, when compared to the Pre-OK model, was observed for the LN model (14% increase in extension, 13% increase in flexion, 5% increase in left bending, 7% increase in right bending, 20% increase in left rotation and 13% increase in right rotation respectively). No noticeable change in the global ROM when compared to the Pre-OK model was observed for the LP model in flexion, extension, left/right bending, and left/right rotation. Reduction in the global ROM, when compared to the Pre-OK model, was observed for the ADF model (55% decrease in extension, 42% decrease in flexion, 55% decrease in left bending, 32% decrease in right bending, 44% decrease in left rotation and 39% decrease in right rotation respectively). Similarly, a decrease in the global ROM when compared to the Pre-OK model was observed for the PDF model (39% decrease in extension, 40% decrease in flexion, 33% decrease in left bending, 47% decrease in right bending, 43% decrease in left rotation and 42% decrease in right rotation respectively). A large decrease in the ROM at the cranial adjacent level compared to Pre-OK model (C2–C3 was observed) for the ADF model in extension (32% decrease) and left bending (36% decrease). For all other cases, the post-operative ROM at C2–C3 was similar to Pre-OK model; the change in ROM was very marginal. At the index levels (C3–C4 and C4–C5), ADF and PDF showed a consistent reduction in ROM when compared to Pre-OK model in all conditions (decrease of larger than 80%). The ROM at these levels was similar to the LP model. On the other hand, the LN model showed a large increase in the ROM at C4–C5 level in all conditions when compared to Pre-OK model. At the caudal adjacent level (C5–C6), the ADF model showed a large reduction in ROM compared to Pre-OK model in extension (30% decrease) and left bending (33% decrease). For all other cases, the post-operative ROM at C5–C6 was similar to Pre-OK model or the change in ROM was very marginal (Fig. 3).

Fig. 3 Range of motion (ROM) in each intervertebral disc in each C3-C5 operation methods. **A** extension, **B** flexion, **C** left bending, **D** right bending, **E** left rotation, and **F** right rotation. The vertical axis is an angle (degree), the horizontal axis is each intervertebral level. And C2-C7 ROM in each motion in each C3-C5 operation method **G**

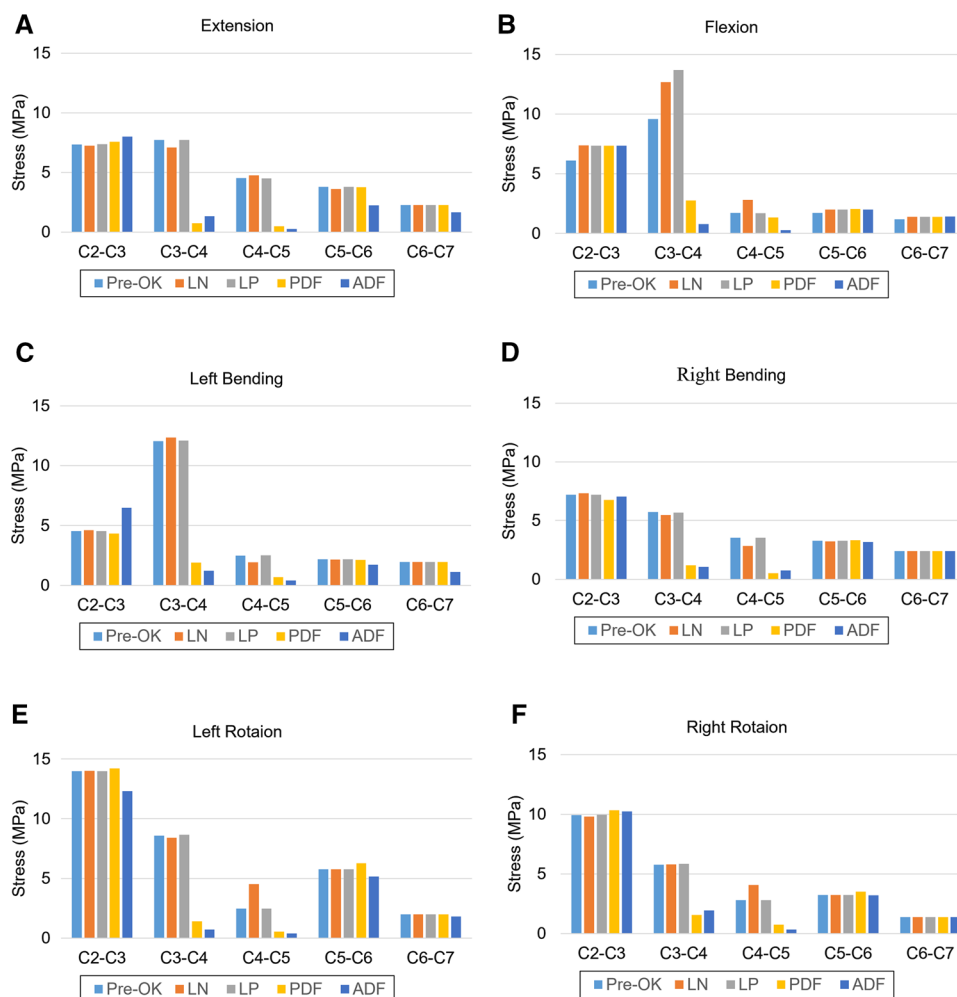


Annular stress

In extension, the C2-C3 (adjacent cranial level) annulus stress of PDF and ADF models increased by 3 and 9% respectively, compared to the Pre-OK model. The C3-C4 annulus stress of LN, PDF, and ADF decreased by 9, 90, and 83% respectively, compared to the Pre-OK model. The C3-C4 annulus stress of LP was the same as Pre-OK model. The C4-C5 annulus stress of LN increased by 5%, LP was the same, and PDF

and ADF decreased by 89 and 94% respectively, compared to the Pre-OK model. The C5-C6 annulus stress of ADF and LN decreased by 41% and 4%, respectively. The C5-C6 annulus stress of PDF and LP was the same as Pre-OK model. In flexion, the C2-C3 annulus stress of LN, LP, PDF, and ADF increased by about 20%, compared to the Pre-OK model. The C3-C4 annulus stress of LN and LP increased by 32 and 43% respectively, compared to the Pre-OK model. The C3-C4 annulus stress of PDF and ADF decreased by 71

Fig. 4 Annular stresses in each C3-C5 operation method. **a** extension, **b** flexion, **c** left bending, **d** right bending, **e** left rotation, and **f** right rotation. The vertical axis is stresses (Mega Pascal; MPa), the horizontal axis is each intervertebral level



and 92% respectively, compared to the Pre-OK model. The C4-C5 annulus stress of LN increased by 62% compared to the Pre-OK model while the annulus stress for LP was similar to Pre-OK. The annulus stress for PDF and ADF in flexion decreased by 22 and 84% respectively, compared to Pre-OK. The C5-C6 annulus stress of LN, LP, PDF, and ADF increased by 15, 15, 19, and 15% respectively compared to the Pre-OK model. A similar trend in annular stress values was observed in left/right bending and left/right axial rotation (Fig. 4).

Nucleus stress

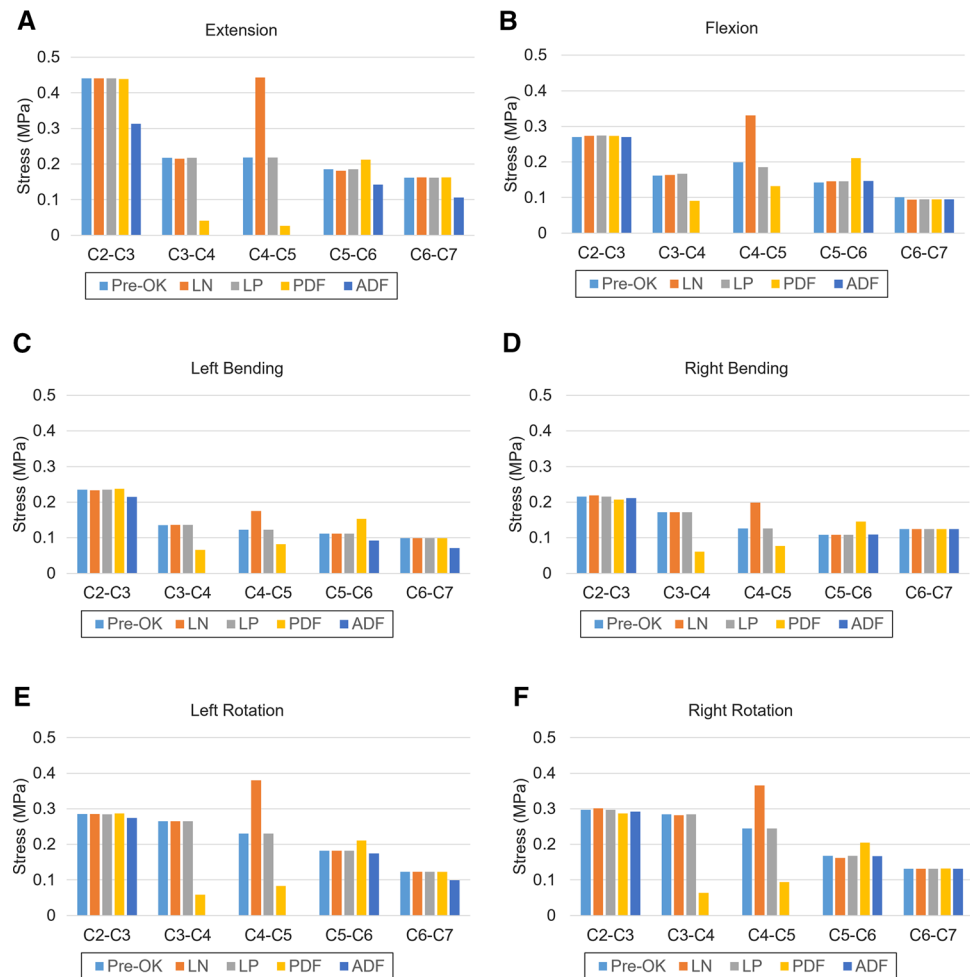
In extension, the C2-C3 nucleus stress of ADF decreased by 29% compared to the Pre-OK model. The C2-C3 nucleus stress of LN, LP, and PDF was almost same in the Pre-OK model. The C3-C4 nucleus stress of PDF was decreased by 81% compared to the Pre-OK model. The C3-C4 nucleus stress of LN and LP was almost same in the Pre-OK model. The C4-C5 nucleus stress of LN increased by 103%, LP was

the same, and PDF decreased by 88% compared to the Pre-OK model. The C5-C6 nucleus stress of ADF reduced by 23%, the C5-C6 nucleus stress of PDF increased by 14% while the nucleus stresses for LN and LP were similar to the Pre-OK model. In flexion, the C2-C3 nucleus stress of LN, LP, PDF, and ADF was almost the same as the Pre-OK model. The C3-C4 nucleus stress of LN and LP was very similar to the Pre-OK model. The C3-C4 nucleus stress of PDF decreased by 44% compared to the Pre-OK model. The C4-C5 nucleus stress of LN increased by 66%. The C4-C5 nucleus stress of PDF decreased by 33% compared to the Pre-OK model. The C5-C6 nucleus stress of PDF increased 48%. A similar trend in nucleus stress values was observed in left/right bending and left/right rotation (Fig. 5).

Facet contact forces

In extension, facet contact forces of the C2-C3 decreased by 73% in ADF, compared to the Pre-OK model. LN, LP, and PDF were almost the same as the Pre-OK model. Facet contact forces of the C3-C4 of LN, LP, PDF, and ADF decreased

Fig. 5 Nucleus stresses in each C3-C5 operation method. **a** extension, **b** flexion, **c** left bending, **d** right bending, **e** left rotation, and **f** right rotation. The vertical axis is stresses (MPa), the horizontal axis is each intervertebral level



by 12, 16, 95, and 99% respectively compared to the Pre-OK model. Facet contact forces of the C4-C5 of LN increased by 545% and LP, PDF, and ADF decreased by 14, 43, and 99% respectively compared to Pre-OK model. Facet contact forces of the C5-C6 of PDF increased by 30% and LN, LP, and ADF decreased by 3%, 16%, and 96% respectively compared to Pre-OK model. In lateral bending and axial rotation, the same trends were showed in flexion (Fig. 6).

Discussion

To our knowledge, the literature lacks mechanical comparisons of the four decompression procedures: LN, LP, PDF, and ADF for kyphotic cervical alignment. This study aimed to investigate the mechanical effects of these surgical procedures for patients with cervical kyphotic alignment using FE analysis.

In clinical research, there are few reports of LP leading to postoperative complications, including instability. There are some reports in the literature analyzing the biomechanical

effects and instability based on the range of the resection of posterior bone and ligament complex of the LN technique using FE [22]. In the clinical history of LP, good results for multi-level decompression have been reported [23]. However, since posterior decompression surgical techniques, such as LN and LP, are invasive on the posterior ligament complex, these procedures may lead to instability in kyphotic cervical alignment and axial pain [24]. Qian reported that LP is not recommended for patients with severe kyphosis and large preoperative ROM [25]. In our analysis, the LN model demonstrated an increased ROM when compared to the Pre-OK model, and the LN and LP models were associated with higher annular stress compared to the Pre-OK model during flexion. On the other hand, Hashiguchi reported in their comparative FE analysis study that LP was more stable than LN [26]. Subramaniam observed in a cadaver study that the open-door LP offered a greater degree of biomechanical stability on the spine than LN which is in agreement with our study which showed a 13% increase in ROM after LN compared to LP during flexion and extension [27]. As in previous reports, our study showed that ROM, annular stress, and the

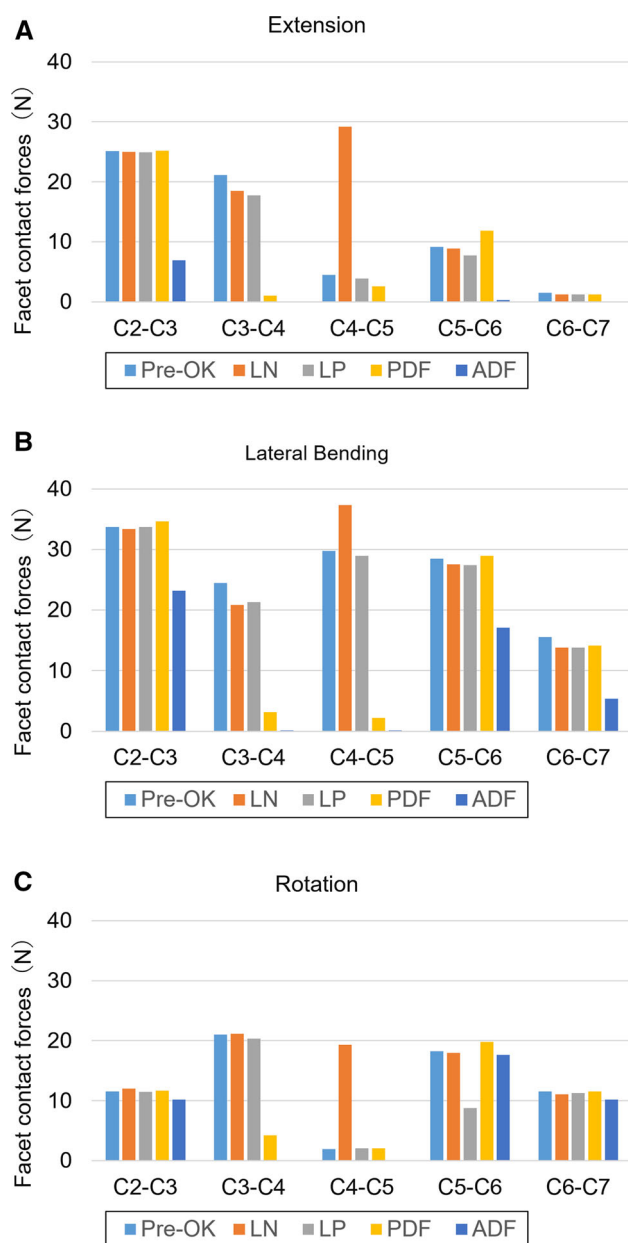


Fig. 6 Facet contact forces in each C3-C5 operation method. **a** extension, **b** lateral bending, **c** axial rotation. Vertical axis is force (N), horizontal axis is each intervertebral level

nucleus stresses for the LN model were much higher than the other models. ROM, annular stress and the nucleus stresses for LP were similar to the Pre-OK model except for flexion.

As a countermeasure to increase in kyphosis due to damage to posterior ligaments in LN and LP, PDF is recommended to prevent post-surgical instability and kyphosis [5]. Kim compared clinical outcomes of standalone LN and PDF in patients with Pre-OK cervical spine and recommended PDF surgery to reduce the risk of progression of postoperative kyphotic deformity [28]. Abumi et al. concluded that PDF provides better clinical outcomes than LP for patients

demonstrating local kyphosis or segmental instability [29]. Papagelopoulos reported that PDF with lateral mass screws provides 98% more stability than LN with facetectomy in a cadaveric model [30]. Though a facetectomy was not performed in our study, we observed 50% higher stability with PDF compared to the LN model in extension, which agrees with the published literature.

ADF typically stabilizes the spinal column at one or two vertebral levels above and below the index segment and is often performed for patients with a cervical kyphotic alignment [31, 32]. Yoshii et al. compared outcomes of ADF and PDF for patients with CSM and found that postoperative cervical alignment was more favorable with ADF than with PDF [6]. In our study, the ADF and PDF models demonstrated a decrease in ROM when compared to LN and LP. Furthermore, PDF and ADF models showed a very large reduction in the annular stresses and the nucleus stresses compared to the other models at the surgery levels in all motions. These results suggest that PDF and especially ADF provide better stabilization of kyphotic cervical alignment compared to LN and LP.

The PDF compensated for resected posterior ligaments by fixation, though the main weakness associated with ADF and PDF is adjacent segmental disease (ASD) [2, 3]. The cervical spine may develop symptoms of ASD if the adjacent segments are associated with high instability and disc stresses [33]. Regarding PDF, the incidence of ASD is estimated to be at 3.4% at 1 year and 5.9% at 2 years [34, 35]. In ADF, the occurrence of radiographic ASD and symptomatic ASD has been reported to be 32.8 and 6.3%, respectively [36]. Li analyzed the risk for the development of ASD, using four FE ADF models, observing that the stresses at the cranial adjacent level increased more than 20% in single cage model [33]. In our study, the caudal adjacent level (C5-C6) nucleus stresses of PDF model showed an increase of about 20% in left/right rotation compared to other models. The adjacent cranial level (C2-C3) annular stresses of ADF models also showed increased of 10% in extension and 40% in left bending compared to other models. The nucleus stresses for the PDF model had increased at the C5-C6 level in all motions. These results suggest that the C2-C3 and C5-C6 adjacent level may be at risk for developing ASD in PDF and ADF models due to rigid fixation. The facet forces for the ADF model were lower when compared to LN and LP models. PDF model had increased facet contact forces at the C5-C6 level. Our results were consistent with the clinical reports suggesting that the LN and LP models are at higher risk for instability, ADF and PDF models are at higher risk for developing ASD complications though has a higher stabilization effect.

There are several limitations to our study such as the model not containing muscle forces. However, the effect of musculature was addressed by the follower load technique [21].

Another point is that the same moment is given as for the Pre-OK model. We have only used one variation of cervical kyphotic alignment without studying the biomechanical effects of cases with higher degree of kyphosis. Our study simulated the immediate postoperative models and did not consider conditions such as fused/un-fused lamina of LP and PDF, fused/un-fused graft bone in ADF and does not fully grasp the long-term biomechanical results of the four surgical techniques. This study did not analyze the case of using a pedicle screw instead of an LMS for PDF. Moreover, the homogenous material properties were assumed in the FE model for different components in the model. Although the effect of aging changes material of bone, this aspect should be explored in future studies to receive more patient-specific or more accurate clinical results. Also, the validated lordotic cervical spine with no surgical intervention had a scoliosis curve that was left-sided. Therefore, despite using the same moment, this is likely the reason for the difference seen in left and right bending. Despite these limitations, our study provides insights into the biomechanical differences among four surgical techniques used for stabilizing kyphotic cervical spine.

Conclusions

We investigated stress changes in the cervical kyphotic model and in four surgical procedures by using FE analysis. This study concluded that posterior decompression, such as LN or LP, is likely to affect ROM, disc stresses, and facet force. Although ASD is a possibility, PDF and especially ADF contributed to more stabilization in kyphosis cases compared to LN and LP.

Declarations

Conflict of interest No benefits in any form have been received or will be acquired by a commercial party related directly or indirectly to the subject of this article.

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