Adjacent Segment Disease

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As a result of reading this article, physicians should be able to:

1. Understand the forces that predispose adjacent cervical segments to degeneration.
2. Understand the challenges of radiographic evaluation in the diagnosis of cervical and lumbar adjacent segment disease.
3. Describe the changes in biomechanical forces applied to adjacent segments of lumbar vertebrae with fusion.
4. Know the risk factors for adjacent segment disease in spinal fusion.

ABSTRACT

Adjacent segment disease (ASD) is a broad term encompassing many complications of spinal fusion, including listhesis, instability, herniated nucleus pulposus, stenosis, hypertrophic facet arthritis, scoliosis, and vertebral compression fracture. The area of the cervical spine where most fusions occur (C3-C7) is adjacent to a highly mobile upper cervical region, and this contributes to the biomechanical stress put on the adjacent cervical segments postfusion. Studies have shown that after fusion surgery, there is increased load on adjacent segments. Definitive treatment of ASD is a topic of continuing research, but in general, treatment choices are dictated by patient age and degree of debilitation. Investigators have also studied the risk factors associated with spinal fusion that may predispose certain patients to ASD postfusion, and these data are invaluable for properly counseling patients considering spinal fusion surgery. Biomechanical studies have confirmed the added stress.

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Spinal fusion has been studied as a means to treat pathology related to the spine for more than a century.\(^1\) Because the proportion of the American population older than 65 years will increase from 12.4% in 2000 to 19.6% in 2030,\(^2\) and due to the many surgical advancements in spinal surgery over the past few decades, the rate of fusion surgeries rose between 1993 and 2003\(^3\) and between 1979 and 1990.\(^4\) Given the current environment, it is imperative that orthopedic surgeons understand the possible outcomes of fusion surgery.

One complication of spinal fusion is adjacent segment disease (ASD) following cervical, lumbar, or lumbosacral fusion. This is a broad term that encompasses symptoms such as listhesis, instability, herniated nucleus pulposus, stenosis, hypertrophic facet arthritis, spondylosis, and vertebral compression fracture.\(^5\) The cause of this degenerative process has been extensively studied in biomechanical studies using animal and cadaver models.\(^6-9\) Whether these degenerative changes also cause clinical, rather than solely radiological, changes has also been studied extensively.\(^10-15\)

Treatment modalities for ASD are complicated by the increased risks associated with revision spinal surgeries and the evolving technology of spinal arthroplasty. Definitive management of ASD continues to be studied, and treatment priorities should be dictated by patient age and the degree of debilitation associated with ASD for each patient. Investigators have also studied the risk factors associated with spinal fusion that may predispose certain patients to ASD postfusion.\(^14,16-25\) These data are invaluable for properly counseling patients considering spinal fusion surgery.

**ADJACENT SEGMENT DISEASE ASSOCIATED WITH CERVICAL SPINAL FUSION Biomechanics**

The motion of adjacent segments after cervical spinal fusion has been modeled in several studies in an attempt to understand the forces that predispose adjacent cervical segments to degeneration.\(^6-9\) The area of the cervical spine where most fusions occur (C3-C7) is adjacent to a highly mobile upper cervical region, and this contributes to the biomechanical stress put on the adjacent cervical segments postfusion. Studies have shown that after fusion surgery, there is increased load on adjacent segments. In a study by Eck et al,\(^6\) six cadaveric spine specimens were tested and stabilized at T1. Pressure increased in both C4-C5 and C6-C7. An image of this experimental apparatus is shown in Figure 1. A finite element model was used by Maiman et al\(^7\) to examine the effects of C4-C5 and C5-C6 fusions, and increased internal stress in adjacent segments was found. Researchers studying a multisegment cervical fusion found that stress on adjacent segments increased between single and double fusions.\(^8\) Lopez-Espina et al\(^8\) used a finite element model and facet-constraining methods to prevent increases in stress. Increases in stress up to 96% were found in the annulus, nucleus, and endplates postfusion. Canine models have also shown a change in proteoglycan population in intervertebral disks postfusion. Cole et al\(^9\) found that the proteoglycan population produced in both the nucleus pulposus and annulus fibrosus postfusion is similar to the proteoglycan population in immature tissue.

**Clinical and Radiographic Diagnosis**

The diagnosis of cervical ASD is complicated given the imprecise correlation of radiographic and clinical findings. Evaluation is difficult because the normal degenerative process in patients is difficult to separate from the effects of the fusion surgery on adjacent segments. No validated classification system exists for cervical ASD.\(^10\) A study by Baba et al\(^11\) followed more than 100 patients for an average of 8.5 years and found an increase in tilting angle in the upper adjacent and lower adjacent segments, as well as newly diagnosed spinal stenosis in 25% of patients.\(^12\) Herkowitz et al\(^13\) prospectively studied 28 patients who had undergone cervical fusion and found that 41% of patients had adjacent level degeneration on radiographs at an average 4.5-year follow-up. Matsumoto et al\(^14\) investigated the use of magnetic resonance imaging (MRI) for ASD by comparing a group of 64 patients undergoing anterior cervical decompression and fusion with 201 asymptomatic vol-
unteers. Disk degeneration at adjacent segments was significantly more likely in the fusion group compared with the control group, although disk degeneration at adjacent segments was not always related to clinical symptoms. Postoperative ASD is shown in Figure 2.

Although the rate of radiographic signs of ASD is high, the rate of clinical symptoms of ASD is lower. Baba et al\textsuperscript{11} retrospectively studied 146 patients undergoing cervical fusion and found that 13.5% of patients had identifiable problems at a level other than the level fused. Lunsford et al\textsuperscript{13} reported a reoperation rate of 10% at a different segment after anterior cervical fusion at less than 3-year follow-up. Hilibrand et al\textsuperscript{14} followed 374 patients over a maximum of 21 years postoperatively and found that symptomatic ASD occurred at a rate of 2.9% over 10 years postoperatively and that 25.6% of patients had ASD within 10 years postoperatively. Yue et al\textsuperscript{15} studied 71 patients undergoing anterior cervical diskectomy and fusion over more than 5 years and found that 16.9% of patients needed revision surgery for symptomatic adjacent level disease, although 73.2% of patients had new-onset or worsening degeneration of disk spaces adjacent to the operated levels.\textsuperscript{15}

**Risk Factors**

Adjacent segment disease only occurs in a certain portion of patients after spinal fusion. Various studies have investigated the risk factors for the development of ASD after cervical spinal fusion. Hilibrand et al\textsuperscript{14} analyzed risk factors that contributed to the progression of symptomatic ASD. Patients who had adjacent segments with neural element compression, surgery at C5-C6 and/or C6-C7 levels, or anterior cervical fusion surgery of more than 1 level were less likely to develop ASD. Williams et al\textsuperscript{16} studied the factors that contributed to positive and negative postoperative outcomes in 90 patients undergoing cervical diskectomy and interbody fusion over 2 to 9 years. Patients with apparently normal preoperative radiographs had worse outcomes than those with osteophyte formation, narrowing of the interspace, or both. Katsuura et al\textsuperscript{17} studied the effect of postoperative malalignment of the cervical spine in a prospective study over 9.8 years and found that 43% of patients with ASD had malalignment of the cervical spine. In patients who have an anterior cervical plate, the distance between the plate and adjacent segments may influence the amount of ossification at adjacent segments. Park et al\textsuperscript{18} found a positive association between plate-to-disk distance and the amount of ossification at adjacent segments.

Two recent systematic reviews specifically studied risk factors related to ASD postoperatively.\textsuperscript{10,19} Lawrence et al\textsuperscript{19} found 5 quality research studies and concluded that fusing segments adjacent to C5-C6 and/or C6-C7 increased the risk of ASD. Of note, the authors mentioned that even after performing a systematic review of more than 170 articles, the development of clinical adjacent segment pathology is difficult to differentiate from the natural history of spinal degeneration. A population-based study from

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**Figure 2:** Adjacent segment disease in the cervical spine. Preoperative radiograph showing disk disease between levels C5-C7 (A). Five-year postoperative radiograph showing fusion of levels C4-C6 with cervical disk space narrowing at C6-C7 (arrow) (B). Five-year postoperative myelography showing intervertebral disk herniation at C6-C7 and complete block of the dural sack at C6-C7 (arrow) (C). Radiograph taken after reoperation for fusion of C6-C7 (D). (Reprinted with permission from Ishihara H, Kanamori M, Kawaguchi Y, et al. Adjacent segment disease after cervical interbody fusion. \textit{Spine J.} 2004; 4[6]:624-628.)
Taiwan noted a low rate of reoperation (0.8%) for clinically significant ASD. Lee et al found that radiographic signs of ASD were more likely in patients who had degenerative indications for cervical spinal fusion.

**ADJACENT SEGMENT DISEASE ASSOCIATED WITH LUMBAR SPINE FUSION**

**Biomechanics**

The fusion of lumbar vertebrae has been associated with changes in the biomechanical forces applied to adjacent segments. The area of adjacent segment biomechanical forces and motion has been studied since the 1980s. In 1984, Lee and Langrana put 16 cadaveric models under combined compression and bending loads to observe motion. They found increased stress on adjacent segments and increased loading on facet joints within unfused segments. Further evidence of facet joint strain postfusion was demonstrated by Ha et al in an experiment with in vitro canine spines. They found increased segmental mobility and changed contact patterns within the joint. Using a finite model, Chen et al also found increased forces in adjacent disks postfusion and noted larger stress increases at the upper adjacent disk rather than the lower disk.

Increased motion at adjacent segments has been postulated as a reason for ASD. Axelsson et al studied 6 patients undergoing radiographic analysis of segment motion before and after L4-L5 fusion surgery. Increased mobility occurred in adjacent segments for 2 of the 6 patients. In an in vivo model, Hayes et al specifically examined mobility and found increased translational motion in adjacent segments when L3-L4 was fused, and this motion correlated with lower back pain. Esses et al studied changes in motion with different fusion techniques in cadaveric models. Posterolateral fusions were found to have less motion in adjacent segments as compared with anterior fusions.

In both cadaveric and finite models, increased intradiskal pressure has been found within adjacent segments. Weinhofer et al studied intradiskal pressure in adjacent segments during flexion in cadaveric models. Intradiskal pressure increased during flexion, and the more segments that were fused, the greater the intradiskal pressure. Similar results were found by Cunningham et al, who studied 11 cadaveric models and found that intradiskal pressure increased by as much as 45%.

Using an in vivo mouse model and a finite element model, Lotz et al studied both the changes in stress in adjacent segments and the biochemical changes within adjacent segments. The finite element model predicted an increase in hydrostatic stress in the middle regions of the annulus by nearly ten-fold. Numerous harmful responses occurred at the histological and cellular levels, including disorganization of the annulus fibrosus, an increase in apoptosis with associated loss of cellularity, and damaging changes in gene expression. In an animal model by Phillips et al, results included loss of chondrocytes.

Figure 3: Radiographs showing progressive changes after lumbar spinal fusion preoperatively (A) and 2 years (B), 5 years (C), and 9 years (D) postoperatively. In this patient, definite signs of adjacent segment disease are present by 13 years after L4-L5 spinal fusion (E). However, it is unclear whether these radiographic changes signify clinical significance. (Reprinted with permission from Cheh G, Bridwell KH, Lenke LG, et al. Adjacent segment disease following lumbar/thoracolumbar fusion with pedicle screw instrumentation. Spine [Phila Pa 1976]. 2007; 32(20):2253-2257.)
and notochordal cells within the nucleus pulposus.

Clinical and Radiographic Diagnosis

Separating the progression of osteoarthritis in patients postfusion from lumbar ASD is difficult. In a study by Kumar et al., patients were followed postfusion with the Short Form 36 and Oswestry Disability Index, functional testing, and radiographs. Their results were compared with those from age- and sex-matched controls. Radiographic changes above the level of fusion were worse in those with fusion compared with those not fused. There was no statistically significant difference in clinical outcomes. Wai et al. studied MRI results over 20 years for patients undergoing lumbar fusion surgery and found that the prevalence of degenerative changes in patients undergoing surgery was similar to age-matched controls. Hambly et al. reported that radiographic changes occur in the transition zone cephalad to lumbosacral fusion, regardless of whether surgery occurred.

As with ASD in the cervical spine, the correlation between clinical, MRI, and radiographic signs of ASD is controversial. Interpretation of radiographic evidence is also complicated by the fact that asymptomatic patients have been found to have substantial abnormalities on MRI. Plain radiographs have been found to be of little help in the diagnosis of ASD. Frymoyer et al. examined plain radiographs from 96 patients who had undergone fusion surgery. Results showed no correlation between radiographic findings and clinical symptoms. The progressive changes seen on radiographs of adjacent segments were illustrated in Figure 3. In the current authors’ experience treating ASD, severe degenerative changes cause symptoms of spinal stenosis. Figure 4 shows an area of neural foraminal narrowing at the L2-L3 level.

Many studies have examined the prevalence of clinical symptoms associated with ASD. In a long-term retrospective study by Ghiselli et al., 215 patients were followed postfusion for an average of 6.7 years. The rate of reoperation at adjacent segments was 16.5% in the first 5 years and 36.1% at 10 years. Similar results were reported by Gillet et al. in a retrospective study that found a reoperation rate of 20% over a range of 2 to 15 years of follow-up. Penta et al. studied MRIs for 10 years after lumbar interbody fusion, and of the 81 patients studied, 32% had radiographically diagnosed ASD. In a large retrospective cohort study by Sears et al. of 1000 consecutive posterior lumbar interbody fusion procedures with a mean follow-up of 63 months, the 10-year prevalence of further surgery for ASD was 22.2%. The annual incidence of surgery for ASD was 2.2%.

The rate of ASD after lumbar fusion varies widely between studies. In a review by Park et al. of 22 studies, the reported range of ASD was 5.2% to 100% based on either radiographic or clinical diagnosis. The authors attributed this wide variation to the range of patient populations, differing clinical or radiographic definitions of ASD, and the retrospective nature of many of the studies.

Risk Factors

Several studies have examined the risk factors that put a portion of patients at risk for ASD. Aota et al. reported that the factor most influential in postfusion instability was age. The study showed that 11 of 30 patients older than 55 years developed ASD postfusion, whereas only 3 of 25 patients younger than 55 years developed ASD postfusion. Similarly, a retrospective study by Etebar and Cahill found that ASD was higher in postmenopausal women. The link between menopause and worsening osteoarthritis is not entirely clear, but active research is ongoing into the mechanism by which a lack of estrogen influences osteoarthritis development and progression. In a retrospective review of 49 patients, Rahm and Hall found that increasing age, as well as interbody fusion, was associated with a higher risk of ASD.
Investigators have studied whether the length of fusion in fusion surgery factors into the development of ASD. Pentà et al\textsuperscript{46} examined MRIs and radiographs from 52 patients who had normal preoperative findings in adjacent levels.\textsuperscript{49} In this group of patients, the length of fusion did not factor into whether ASD occurred. Wimmer et al\textsuperscript{51} studied the effect of polysegmental fusions on anteroposterior translation in 120 patients with painful spondylolisthesis who were treated with combined anterior and posterior fusions. The study group was divided into a monosegmental fusion group (n=46) and a polysegmental fusion group (n=74). Polysegmental fusion was associated with a greater degree of anteroposterior translation.

Fusion involving the L4-L5 segment has been cited as a possible cause of disk degeneration at L5-S1. This was specifically studied by Ghiselli et al\textsuperscript{52} in a group of 32 patients over 7.3 years. Their investigation found a general progression of degenerative changes in the L5-S1 segments. However, the authors concluded that there was no need for routine fusion of L5-S1 in patients with isolated L4-L5 symptoms.

Another significant factor in determining ASD postfusion is the anatomical alignment of spinal segments preoperatively. Investigators have noted increased ASD in patients with a preoperative L1 and S1 axis distance greater than 35 mm.\textsuperscript{51} In a retrospective study, Kumar et al\textsuperscript{51} reported that patients with a normal C7 plumb line and sacral inclination had the lowest rate of ASD. In a study by Lazennec et al\textsuperscript{54} of 81 patients who had undergone fusion, there was a statistically significant relationship between postoperative pain and sacral tilt. Oda et al\textsuperscript{55} used a sheep model to determine the biomechanical changes in adjacent segments in kyphotic spines. Results showed that kyphotic posterolateral fusion significantly altered supra-adjacent segments by inducing more stiffness in the posterior ligamentous complex and increasing lamina strain under flexion-extension loading. There were significant degenerative changes in the supra-adjacent segments in these sheep. Lehmann et al\textsuperscript{56} found a correlation between preoperative segmental instability in the segment above fusion and lumbar spinal stenosis. The greater the translation instability, the more likely the adjacent segment would become unstable post-fusion. Biomechanical studies have also shown that once degeneration occurs at one segment, the risk of degeneration at other adjacent segments increases.\textsuperscript{57} Schlegel et al\textsuperscript{58} reported that segments that were 2 segments removed from fusion were just as likely to show degeneration as adjacent segments.

The alignment of fusion in the lumbar spine was investigated in a biomechanical cadaveric study by Akamaru et al.\textsuperscript{59} They reported that fusion in either hyper- or hypolordotic alignment of L4-L5 resulted in different loads on adjacent spinal segments. Hypolordotic alignment of L4-L5 resulted in the greatest amount of flexion-extension motion at L3-L4, whereas hyperlordotic alignment of L4-L5 resulted in the greatest amount of flexion-extension motion at L5-S1. In a study of patients undergoing 360° fusion with healthy adjacent segments preoperatively, it was found that maintaining the lordotic angle at approximately 20° postoperatively was associated with the prevention of ASD.\textsuperscript{60}

Several studies have investigated ASD in the lumbar spine following different treatment decisions. In a prospective study of 111 patients with spondylolisthesis who were randomized to exercise, uninstrumented posterolateral fusion, or instrumented posterolateral fusion, accelerated adjacent segment degeneration was found in the patients that had fusion and laminectomy.\textsuperscript{61} Abdu et al\textsuperscript{52} studied 380 surgical candidates with degenerative spondylolisthesis who underwent 1 of 3 surgical interventions: posterior in situ fusion, posterolateral instrumented fusion with pedicle screws, or posterolateral instrumented fusion with pedicle screws plus interbody fusion (360°). At 3- and 4-year follow-up, there was no statistical difference in outcome criteria (ie, Short Form 36 bodily pain, physical function scales, and the modified Oswestry Disability Index) between the different operative techniques. Furthermore, in a randomized, controlled trial performed by Videbaek et al.,\textsuperscript{63} patients who underwent anterior lumbar interbody fusion combined with posterolateral lumbar fusion or posterolateral lumbar fusion alone showed no increased risk of ASD. Therefore, it does not appear that a specific treatment technique accelerates the onset of increases the likelihood of developing ASD compared with any other.

Edwards et al\textsuperscript{64} investigated long adult fusions of the thoracolumbar spine to L5 and the resultant degenerative changes to S1. Thirty-four patients were followed for a mean of 5.6 years. Results showed that 61% of patients had resultant degenerative disk disease. Risk factors for degenerative changes were a positive sagittal balance, younger age at operation, and any signs of radiographic degeneration at L5-S1.

Added instrumentation during spinal fusion has been studied as a possible risk factor for ASD. Shono et al\textsuperscript{65} investigated whether fusion surgeries augmented with instrumentation such as a compression hook and a transpedicular screw fixation system increased motion in adjacent segments. The study was conducted with a calf lumbarosacral spine model. As spinal instrumentation increased, higher segmental displacement occurred at the upper residual intact motion segment. Interestingly, different results were reported by Wiltse et al\textsuperscript{66} with the use of pedicle screws. They studied pedicle screws and their relationship to transition zone changes above or below the fused segment. No increase in ASD incidence was found with pedicle screw placement.
Ahn et al\textsuperscript{60} retrospectively studied 3188 patients who underwent thoraco-lumbar spinal fusion to find the rate of ASD, as well as risk factors. Results showed a failure rate of 6% at 10 years at adjacent segments. Risk factors noted were multiple level fusions, old age, degenerative disease prior to fusion, and male sex. A study by Lee et al\textsuperscript{61} investigated overall risk factors for revision surgery due to ASD. Of 1069 patients undergoing spinal fusion surgery, 2.62% required revision surgery. Postoperative facet degeneration was associated with revision surgery, and the incidence of ASD in proximal segments was found to be higher than that in more distal segments. Preexisting degeneration was found to be a significant risk factor for ASD requiring surgery.

The intraoperative decision of distracted disk height of the fused segment caused by cage or bone insertion has been studied as a risk factor for ASD. Kaito et al\textsuperscript{62} studied 84 patients with L4 spondylolisthesis who were treated with posterior lumbar interbody fusion. Patients who developed ASD were found to have higher L4-L5 disk space distraction.

Nassr et al\textsuperscript{63} investigated whether incorrect needle localization during anterior cervical diskectomy and fusion caused ASD. Of 87 patients undergoing anterior cervical diskectomy and fusion, 15 had incorrect needle localization. The group with incorrect needle localization was associated with a 3 times higher rate of ASD. The authors concluded that either needle trauma or unnecessary surgical dissection may have caused ASD during the study. A recent systematic review for risk factors for ASD after lumbar fusion showed that age older than 60 years was associated with an increased risk of ASD after spinal fusion.\textsuperscript{19} Similarly, if the patient had preexisting facet degeneration, degenerative disk disease, multilevel fusion, laminectomy performed adjacent to a segment, a construct stopped at L5, or excessive disk height distraction, then the risk of ASD may be higher.

**TREATMENT**

There is no gold standard treatment for ASD, but there are methods to treat its symptoms. Several studies have shown that treatment with decompression of neural elements with possible extension of fusion may relieve symptoms.\textsuperscript{31,69,70} Although there seems to be some pain relief with extension of fusion, these studies showed that extension of fusion may result in higher rates of ASD in the newly created adjacent segments. These studies reported significant complication rates, and the number of treated patients was small. Arthroplasty has been promoted as a potential solution to ASD, but results from numerous studies indicate that more data are needed to ensure improved clinical outcomes.\textsuperscript{71-76} An example of a total disk arthroplasty device is shown in Figure 5.\textsuperscript{77} A recent Cochrane review showed that although there was a statistically significant improvement in outcome measures associated with total disk arthroplasty, it was not clear whether this difference was clinically significant.\textsuperscript{78} The authors of the review emphasized caution in adoption of the new technology.

**CONCLUSION**

Adjacent segment disease is a complication related to spinal fusion. Its diagnosis is clouded by the fact that many patients have underlying degenerative changes that may mimic ASD. Biomechanical studies have confirmed the added stress on adjacent segments in the cervical and lumbar spine. Although radiological and clinical diagnoses do not always correlate, radiographs and clinical examination dictate how a patient with prolonged pain is treated. Options for both cervical and lumbar spine ASD include fusion and/or decompression. Although current studies are encouraging regarding the adoption of arthroplasty in spinal surgery, more long-term data are required for full adoption of arthroplasty as the standard of care for the prevention of ASD.

**REFERENCES**


