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REVIEW

Adjacent segment degeneration after fusion spinal surgery—a systematic review

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Abstract

Purpose Adjacent segment degeneration (ASDeg) and disease (ASDis) have become major concerns after fusion surgery. However, there is no definitive data or knowledge about the incidence or risk factors. The review discusses the incidence and risk factors and prevention of ASDeg and ASDis in the relevant literature.

Methods We performed a systematic review of meta-analyses, randomized control trials, and cohort studies published in English to provide evidence-based information about ASDeg and ASDis.

Results According to a meta-analysis, the pooled incidence of ASDeg after lumbar and cervical fusion surgery was 26.6% and 32.8%, respectively. Approximately 1/4–1/3 of ASDeg progressed to ASDis. Risk factors after cervical fusion surgery were young age, pre-existing disc degeneration, short fusion segment, high T1 slope, disruption of adjacent soft tissue, and plate placement close to the adjacent disc. The risk factors of ASDeg and ASDis after lumbar fusion surgery were age, genetic factors, high body mass index, pre-existing adjacent segment degeneration, laminectomy at the adjacent level of fusion, excessive distraction of the fusion level, insufficient lumbar lordosis, multilevel fixation, floating fusion, coronal wedging of L5-S disc, pelvic tilt, and osteoporosis. Motion-preserving surgeries seem to have less risk of ASDeg and ASDis than conventional fusion surgery both in the lumbar and cervical spine.

Conclusions The existent literature points out variables involved in ASDeg and ASDis. High evidence-level studies should provide more relevant data to guide strategies for avoiding ASDeg and ASDis.

Keywords Adjacent segment degeneration · Adjacent segment disease · Fusion surgery · Lumbar spine · Cervical spine

Introduction

The number and the rate of spinal fusion surgeries have been increasing annually [1, 2]. Recently, adjacent segment degeneration (ASDeg) has become a major concern after fusion surgery. Adjacent segment degeneration is defined as the radiographic change in the intervertebral discs adjacent to the surgically treated spinal level, regardless of the presence of symptoms [3]. Adjacent segment disease (ASDis) represents symptomatic adjacent segment degeneration, causing pain or numbness due to post-operative spinal instability or nerve compression at the same level [4]. The relationship between adjacent segment degeneration and spinal fusion surgery has been discussed in several reports [4, 5]; however, no definitive data or knowledge about the incidence or risk factors exist due to various operative methods or patients' backgrounds. As a matter of course, the pathology of adjacent segment degeneration differs between the lumbar and the cervical spine due to the difference in their anatomical and mechanical feature. Although various new surgical strategies have been developed to avoid adjacent segment degeneration (especially for motion-preserving surgeries) [4, 6–8], the efficacy of those new technologies is still controversial.

This review aims to discuss the incidence and risk factors of and methods to avoid adjacent segment degeneration and disease in the lumbar and cervical spine in reference to recent literature.

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Incidence

The incidence of ASDeg and ASDis after spinal fusion surgery has a great variance among previous reports. Xia et al. [9] analyzed ASDeg and ASDis by meta-analysis using 94 literature reports containing 34,716 patients who underwent spinal fusion surgery.

According to their report [9], the occurrence of ASDeg and ASDis after lumbar spinal fusion surgery ranges 5–77% and 0–27% with a pooled prevalence of 26.6% and 8.5%, respectively. On the contrary, the occurrence of ASDeg and ASDis after cervical spinal fusion surgery ranges 7–92% and 0–25% with the pooled prevalence of 32.8% and 6.3%, respectively. Table 1 shows the prevalence of ASDeg and ASDis by spinal level. The prevalence of ASDeg and ASDis was also analyzed by period from the spinal fusion surgery. The post-operative period was divided into three groups for the analysis: 0.5–two, two to five, and five to ten years. Table 2 shows the prevalence of ASDeg and ASDis in each period. Hilibrand et al. [10] reported that the ASDis after cervical anterior arthrodesis occurred at a relatively constant incidence of 2.9% per year, reaching 25.6% after ten years. Considering these data, approximately 1/4–1/3 of ASDeg is assumed to proceed to ASDis; radiographic adjacent segment degeneration is not necessarily related to symptoms after spinal fusion surgery, as shown in the literature [11–13].

Natural course, biomechanics, and risk factors

Adjacent segment degeneration and disease after spinal fusion surgery are considered to be multifactorial. Since the biomechanical feature is different by the levels of the spinal column, the etiology and/or risk factors are likely also different between the lumbar and cervical spine.

Lumbar spine

Natural course and non-fusion surgery

Regarding the natural course of disc degeneration, a study of whole spine magnetic resonance images (MRI) of 653 patients revealed that the grade of disc degeneration is strongly correlated with aging in all levels of the spine [14]. Age-related lumbar intervertebral disc degeneration was also reported in healthy volunteers [11, 13, 15]. According to these reports, more than half of healthy individual ≥ 60 years have degenerated discs, determined radiologically. On the contrary, the cumulative incidence of ASDis after lumbar laminectomy without fusion was reported to be 10% over four years [16], which was lower than that with fusion surgery at the same institute [17].

Table 1 Incidence of ASDeg and ASDis after spinal fusion surgery by spinal level (Xia et al. [9])

	Lumbar	Cervical
ASDeg	26.6% (21.3–31.9%)	32.8% (17.8–47.9%)
ASDis	8.5% (6.4–10.3%)	6.3% (4.8–7.8%)

ASDeg adjacent segment degeneration, *ASDis* adjacent segment disease. Numbers in brackets indicate 95% confidence interval

Biomechanics

In a biomechanical study using finite element models, fusion at the L4/5 level increased stress on L3/4 vertebral endplate and intervertebral discs on flexion/extension moment [18]. Also, a cadaveric experiment revealed the increased intradiscal pressure of the adjacent, proximal intervertebral disc to the fixed level [19, 20]. Cunningham et al. demonstrated increased L2/3 intradiscal pressure on flexion/extension stress by 45% in the cadaveric L3/4 fixation model [19].

Risk factors

Various risk factors have been proposed on the occurrence of ASDeg or ASDis and were discussed in the literature, such as aging, genetic factors, high body mass index (BMI), pre-existing adjacent segment stenosis or degeneration, laminectomy at the adjacent level of fusion, excessive distraction of the fusion level, insufficient lumbar lordosis, multilevel fixation, "floating fusion" with the lower end vertebra of the fusion at L5, coronal wedging of L5-S disc, posterior tilting of the pelvis, and osteoporosis (Table 3). Lawrence et al. [21] stated that patients older than 60 years may have an increased risk of developing ASDis in the lumbar spine. A genetic investigation revealed that single-nucleotide polymorphisms in the *IL18RAP* gene were associated with lower disc space height at the adjacent level, although this relationship has not been replicated [22]. Retrospective studies investigating a relationship between BMI and ASDeg demonstrated the higher incidence of ASDeg in patients with BMI ≥ 25. Pre-existing adjacent segment narrowing, degeneration of intervertebral disc, and facet joint are also risk factors of ASDis [23–25]. According to Yugue et al. [25], spinal canal narrowing at an adjacent segment ≥ 47% was found to be a risk factor of ASDis following lumbar fusion surgery. Additionally, laminectomy at the adjacent level of fusion increases the risk of ASDeg. Miyagi et al. [26] stated that the rate of ASDeg was significantly higher at the decompressed site adjacent to the fused level in patients with posterior lumbar interbody fusion (PLIF) compared to those without decompression. Radcliff et al. [27] also supported the finding of risk of ASDis after laminectomy of adjacent level. Kaito

Table 2 Incidence of ASDeg and ASDis after spinal fusion surgery by postoperative period (Xia et al. [9])

	0.5–2 years	2–5 years	5–10 years
ASDeg	21.8% (16.0–27.6%)	33.6% (21.8–45.4%)	37.4% (10.7–64.1%)
ASDis	6.5% (4.8-8.1%)	12.1% (8.2-16.0%)	3.2% (2.5-4.0%)

ASDeg adjacent segment degeneration, *ASDis* adjacent segment disease. Numbers in brackets indicate 95% confidence interval

et al. [28] observed the relationship between the extent of disc space distraction of L4/5 disc and occurrence of ASDeg and ASDis at the L3/4 disc in patients with L4/5 PLIF. The L4/5 disc space distraction by cage insertion was 3.1 mm in the group without ASDeg, 4.4 mm in the group with ASDeg, and 6.2 mm in the group with ASDis. They concluded that the excessive distraction of the fusion level by cages was a significant risk factor of ASDeg and ASDis. Sagittal malalignment or loss of lumbar lordosis after lumbar fusion surgery was discussed by Djurasovic et al. [29] in their case-control study. Patients who required re-operation for ASDis had significantly less lordosis through the fused levels and total lumbar lordosis. The number of fusion levels can also influence the occurrence of ASDeg. The longer lever arm produced by multiple-level fusion causes more stress at the free segments [30]. The influence of floating fusion, i.e., fusion with the lower end vertebra at L5, on ASDis was investigated in a retrospective study with a large case series from a single institute by Bydon et al. [17]. In 511 cases of posterolateral instrumented lumbar arthrodesis, floating fusion cases were more likely to develop ASDeg. Moreover, coronal wedging of the L5/S disc is also a risk factor of foraminal stenosis at L5/S level after floating fusion [31]. High pelvic tilt is also a potential risk factor of ASDeg. In a retrospective study of 263 patients with transforaminal lumbar interbody fusion, logistic regression and receiver operating characteristic analyses revealed that the risk of ASD incidence was 5.1 times greater in subjects with pre-operative PT of more than 22.5% [32]. Another retrospective study demonstrated that patients with a sacral slope (SS) < 39° or PT > 21° were at higher risk for ASDis, with a relative risk of 1.73 and 3.66, respectively [33]. Osteoporosis is another potential risk of ASD. In an experiment with spinal fusion in ovariectomized, osteoporotic rat model, osteoporosis evoked greater ASDeg than wild-type rats, which was prevented with the administration of alendronate [34]. A similar effect was observed by administration of parathyroid hormone (PTH) 1-34 in another experiment using rat models [35].

Table 3 Risk factors of ASDeg and ASDis after lumbar and cervical fusion surgery

Lumbar	Cervical
Age (≥ 60 years)	Age (≤ 40 years)
Genetic factors	Preexisting disc degeneration
High body mass index	Short fusion segment
Preexisting ASD	High T1 slope
Laminectomy at adjacent level of fusion	Disruption of adjacent soft tissue
Excessive distraction of the fusion level	Plate placement close to adjacent disc (≤ 5 mm)
Insufficient lumbar lordosis	
Multilevel fixation	
Floating fusion (multilevel fixation with lower end-vertebra of L5)	
Coronal wedging of L5-S disc	
Posterior tilting of the pelvis	
Osteoporosis	

ASDeg adjacent segment degeneration, *ASDis* adjacent segment disease

Cervical spine

Natural course and non-fusion surgery

Regarding the natural course of the cervical intervertebral disc, Boden et al. [36] investigated MRI of the cervical spine in 63 asymptomatic volunteers without previous history of cervical disorders. Major abnormalities in the cervical intervertebral discs were found in 14% and 28% of the subjects younger than 40 and elder than 40 years, respectively. Kretzer at al. [37] reported a cadaveric study measuring range of motion and intradiscal pressure in adjacent discs in various patterns of posterior surgeries for the cervical spine. In a study comparing C3–C6 laminectomy with/without posterior instrumented fusion, posterior instrumentation doubled both the range of motion and the intradiscal pressure of the adjacent discs.

Biomechanical studies

In a biomechanical study using a finite element model [38], C5/6 fixation caused higher stress force on C4/5 disc more than C4/5 fixation on the C5/6 disc, indicating the upper adjacent segment to the fixation site received more stress force than the lower adjacent segment. A cadaveric study also demonstrated that anterior cervical fusion caused increased intradiscal pressure in the proximal adjacent disc on flexion/extension [39]. Matsumoto et al. [40] compared disc degeneration on MRI between patients with anterior cervical fusion surgery and normal volunteers. The study demonstrated the decreased signal intensity of C4/5, increased posterior protrusion of C5/6 disc, decreased disc height, and progressed foraminal stenosis at C3/4 and C6/7 disc in fusion group; however, these changes were not necessarily symptomatic.

Risk factors

The features of risk factors of ASDeg and ASDis in cervical spine differ from those in the lumbar spine, due to the difference in anatomical structure and/or mechanical function. In the cervical spine, young age, preexisting disc degeneration, short fusion segment, high T1 slope, disruption of adjacent soft tissue, and plate placement close to the adjacent disc are proposed to be potential risk factors causing ASDeg and ASDis (Table 3). Lawrence et al. [41] reported that in people aged less than 60 years, pre-existing disc degeneration and fusion adjacent to C5–6 and/or C6–7 levels contribute to the development of ASDis. Interesting findings have been shown in the literature for the incidence of ASDeg after single-level and multiple-level cervical fusion. Ikenaga et al. [42] reported that a ten year follow-up of 31 cases after > four level cervical anterior fusion showed only one case of ASDeg, indicating that the cervical anterior multilevel fusion is not necessarily a risk factor. Hilibrand et al. [10] also demonstrated that the risk of ASDis following multilevel cervical fusion was significantly lower than that following single-level fusion. In this study, 31 out of 256 multilevel fusions and 27 out of 153 single-level fusions caused ASDis (odds ratio, 0.64; $P < 0.001$). Yang et al. [43] assessed the impact of T1 slope on the development of ASDis. While analyzing 90 cases with cervical disc arthroplasty (CDR), the incidence of symptomatic adjacent segment degeneration and neck pain was significantly more severe in patients with high T1 slope. Nassr et al. [44] analyzed the influence of soft tissue disruption in anterior cervical fusion surgery, finding that 15 of 87 patients with anterior cervical discectomy and fusion had incorrect needle localization, i.e., a needle was placed at the level not included in the fusion at surgery. Patients with incorrect needle localization developed more disc degeneration at the two year follow-up with an odds ratio of 3.2. They concluded that needle penetration of nucleus pulposus could facilitate disc degeneration. Plate placement close to the adjacent disc is also reported as a risk factor of ASDis. Park et al. [45] reviewed lateral radiographs of 118 patients with cervical anterior fusion with a plate and found that the adjacent disc ossification occurred more frequently in patients whose plate placement was within 5 mm of the adjacent disc. The risk factors of ASDeg and ASDis in occipitocervical fusion surgery were also discussed. In the retrospective study of 41 non-rheumatoid arthritis patients with atlantoaxial instability, Wu et al. [46] found that patients with ASDeg had less correction of O-C2 angle and C2-7 lordosis compared to those without ASDeg, and concluded that the poor correction of cervical sagittal alignment could be a risk factor in developing ASDeg and ASDis.

Strategies to avoid adjacent segment degeneration and disease

Spinal fusion surgery develops adjacent segment degeneration by concentrating a stress force in the adjacent segment, regardless of the presence of concomitant symptoms [3]. In this regards, strategies to avoid adjacent segment degeneration are discussed in this section, especially highlighting tips in conventional fusion surgery and effect of recent motion-preserving surgery in the lumbar and cervical spine.

Lumbar spine

Several tips have been proposed for conventional lumbar fusion surgery to prevent adjacent segment degeneration. Liu et al. [47] conducted a clinical research study to elucidate the effect of posterior element resection in lumbar fusion. In total, 120 patients were randomly allocated for facetectomy, hemilaminectomy, and total laminectomy on L4-5 fusion. After asix year follow-up, patients with total laminectomy developed a significantly larger number of ASDeg and ASDis cases. Imagama et al. [48] also investigated the effect of laminectomy on fusion level. A five year follow-up of 52 patients after L4-5 fusion with L4 laminectomy or L4-5 fenestration revealed that patients with fenestration developed less ASDeg. Results indicate that preservation of posterior element of the fusion site is a key factor to avoid ASDeg or ASDis after lumbar fusion surgery. Makino at al. [49] reported that minimum disc distraction using low-profile interbody cages could prevent ASDeg. In that study, the incidence of ASDeg in 41 patients with L4-5 PLIF with minimum disc distraction (12.2%) was significantly lower than that of previous study about PLIF with distracted disc space (31.8%). Treatment of osteoporosis is another tip to prevent ASDeg and ASDis. An experiment with a lumbar fusion model of ovariectomized rats demonstrated significantly more ASDeg than a control group, and the administration of alendronate significantly improved bone mass and vertebrae microstructures, increased disc height, and decreased endplate calcification area. Additionally, alendronate significantly decreased *COL1*, *MMP13*, and *ADAMTS4* expression and increased *COL2* and aggrecan expression in the disc matrix [34]. The same group showed that parathyroid hormone (PTH) 1-34 in the same model also prevents ASDeg by preserving disc height, microvessel density, relative area of vascular buds, endplate thickness, and relative area of endplate calcification [50]. These results suggest the use of bisphosphonates or PTH in patients with lumbar spinal fusion surgery.

Recently, motion-preserving techniques such as total disc arthroplasty have been developed and widely used under the belief that preserved segmental motion could disburse the stress on the adjacent segments. On the contrary, the adjacent segment degeneration-prevention effect of total disc arthroplasty has been controversial. Among recently published meta-analyses comparing the incidence or risk of ASDeg or ASDis between conventional lumbar fusion surgery and motion-preservation procedures, Pan et al. [51] analyzed 15 studies, including nine cohort studies and 6 randomized controlled trials (RCTs), comprising 1474 patients. Among these patients, 687 underwent fusion and 787 underwent motion-preservation procedures. The prevalence of ASDeg after long-term follow-up in lumbar fusion group (37.5%) was significantly higher than that in the non-fusion group (18.6%) with an odds ratio of 3.03. Also, the prevalence of ASDis in the fusion group (14.4%) was significantly higher than that in the motion-preserving group (5.1%) with an odds ratio of 2.81. The re-operation rate in the fusion group (7.7%) was also significantly higher than that in the motion-preserving group (1.1%) with an odds ratio of 4.82. From the viewpoint of ASDeg and ASDis risk, motion-preserving surgery appears to be superior to fusion surgery, although each procedure should consider the pros and cons in other parameters.

Cervical spine

Considering that multiple cervical anterior fusions do not increase the risk of ASDeg and ASDis compared to single-level fusion [10, 52], Basques et al. [52] concluded that well-preserved cervical alignment contributes to lower incidence of adjacent segment problems. Therefore, ACDF with well-preserved cervical lordosis could help to avoid ASDeg and ASDis. Nassr et al. [44] reported that incorrect needle placement into the disc increases the risk of ASDeg as shown in the risk factor section, indicating that preservation of adjacent soft tissue could help ACDF to avoid ASDeg and ASDis.

As total disc replacement or cervical disc arthroplasty (CDR) has been used worldwide recently, cohort studies and RCTs have reported this new technique. Among meta-analyses investigating the incidence of ASDeg and ASDis between these procedures, the largest and most recent study was conducted by Dong et al. [53]. In this analysis, 41 articles including 27 RCTs, eight retrospective cohort studies, and six prospective cohort studies were enrolled containing a total of 3959 patients with CDR and 3573 patients with ACDF. The rate of ASDeg was 60% lower in CDA compared with ACDF, with an odds ratio of 0.40. In subgroup analysis, the rate of ASDeg in single-level and 2-level CDA was 54% and 74% lower than that of ACDF, respectively. Also, the rate of ASDis was 50% lower in CDA than ACDF. The rate of reoperation for ASDis was reduced by 47% in the CDA group compared to ACDF, with an odds ratio of 0.53. Especially in patients with 24-month or longer follow-up, the re-operation rate was reduced by 69% in the CDA group (odds ratio, 0.31). Moreover, the range of motion of upper and lower adjacent disc was significantly reduced compared to ACDF. Accordingly, motion-preserving cervical surgery seems to have potential preventing ASDeg and ASDis by reducing mechanical stress to the adjacent disc. These results are consistent with Hilibrand's study [10] stating a close correlation between the incidence of ASDis and the magnitude of motion at the adjacent disc level.

Conclusion

The aetiology, incidence, and risk factors of adjacent segment degeneration and disease in various fusion surgeries are gradually being elucidated. In particular, meta-analyses of RCT and retrospective/prospective cohort studies have formed strong evidence. However, owing to the multifactorial feature of adjacent segment degeneration and disease, a variety of surgical options is challenging to give consensus on pathology or risk factors. The risk factors of adjacent segment degeneration and disease were different between the lumbar and cervical spine because of the difference in their mechanical and functional feature. Strategies to avoid adjacent segment problems in the lumbar spine include minimal disc space distraction for cage placement and preservation of adjacent posterior elements. Additionally, motion-preserving technologies such as total disc arthroplasty have been widely used in both lumbar and cervical spine. Studies have determined a potential to decrease adjacent segment problems by diverging stress forces on the adjacent segments. Further studies generating high evidence-level need to provide more precise and concrete data to inform strategies avoiding ASDeg and ASDis in spinal surgeries.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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