REVIEW ARTICLE

New progress in adjacent segment degeneration/disease

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Adjacent segment degeneration/disease (ASD) has been generally accepted as a long-term complication after spinal surgery. Although the incidence of ASD is not very high, it is gradually recognized to be a very important factor in evaluation of the long-term effect of spinal fusion. There are many views concerning pathogenic factors and ways of prevention and treatment. The authors review and discuss the current research and this article will describe recent advances in ASD.

Key words: Postoperative complications; Spinal diseases; Spinal fusion

Introduction

The concept of spinal segment arthrodesis as a treatment for pathologic conditions of the human spinal column evolved almost 100 years ago. Spinal fusion was first described by Albee for the treatment of Pott's disease¹, and then by Hibbs², who performed spinal fusion as a treatment for spinal deformity. Over the last 50 years many authors have used cervical spine fusion as a treatment for degenerative spondylotic conditions³, and it has become the standard of care for numerous pathologic conditions of the spine. In the cervical spine, decompression and fusion have provided a greater than 90% likelihood of relieving radicular symptoms and stabilizing or improving myelopathy^{4,5}. Posterior lumbar interbody fusion (PLIF) with pedicle screw fixation, a standard form of surgical management of lumbar spondylolisthesis resulting in segmental instability or symptomatic compression of neural element and unresponsive to conservative treatment, has been widely used and has produced some satisfactory clinical results⁶. However, since over the past two decades spinal fusion has been performed on younger patients and the rates of cervical and lumbar spine surgery have increased, concern regarding the effect on the mobility of adjacent segments has been increasing. It is now generally accepted that adjacent segment degeneration/disease (ASD) has become a long-term complication which may require additional surgical inter-

vention^{7,8}. The term ASD can be used to describe radiographic changes seen at levels adjacent to previous spinal fusion procedures that do not necessarily correlate with any clinical findings. On the other hand, the term ASD also refers to the development of new clinical symptoms that relate to spinal fusion⁹. This article will consider advances in the understanding of ASD.

Incidence

Suratwala and his associates studied a total of 80 adult patients who met the inclusion/exclusion criteria for multilevel (three or more motion segments) 360° fusion for lumbar degenerative disc disease¹⁰. ASD was noted in 11 patients (13.75%) after a minimum of 2 years' follow-up. Of these, 5 (6.25%) had undergone an extension of their fusion within the study period. Ghiselli *et al.* analyzed a group of 215 patients who had undergone posterior lumbar arthrodesis an average of 6.7 years previously¹¹. Fifty-nine (27.4%) of them had evidence of degeneration at the adjacent levels and elected to have an additional decompression (15 patients) or arthrodesis (44 patients). Kaplan-Meier analysis predicted a disease-free survival rate of 83.5% (95% confidence interval, 77.5%–89.5%) at five years and of 63.9% (95% confidence interval, 54.0%–73.8%) at ten years after the index operation. Katsuura *et al.* noted degenerative changes on radiological examination in levels adjacent to a fused segment in 21 of 42 patients (50%), following anterior cervical interbody fusion, at 9.8 years average follow-up¹². Hilibrand *et al.* demonstrated that symptomatic ASD may affect more than one-fourth of all patients within ten years after cervical arthrodesis, as defined by the presence of new radiculopathy or myelopathy referable to an adjacent motion segment¹³. The study demonstrated an annual

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incidence of symptomatic disease of approximately 2.9% following the index procedure. Levin *et al.* reviewed a number of articles and estimated that, following anterior cervical discectomy and fusion, the incidence of radiographic adjacent segment degeneration in the cervical spine was between 5% and 9% per year, however, symptomatic ASD appeared to occur at a rate of 2% to 3% per year¹⁴.

Although the incidence of adjacent segment degeneration and disease is not very high, ASD has gradually been recognized to be a very important factor in evaluation of the long-term effect of spinal fusion.

Factors

Sagittal alignment is generally accepted to be one of the most important factors that affect the occurrence and development of ASD. Chen *et al.* compared adjacent lumbar joint mobility of three sagittal alignments in a porcine model¹⁵. Their results implied that an instrumented spine in lordosis is less likely to develop adjacent instability than a kyphotic spine in the superior segment, but not in the inferior. Cho *et al.* allocated their 45 patients to two groups according to whether their L₅-S₁ segments had been fused¹⁶. After a minimum of 2 years' follow-up they found that, for patients with sagittal imbalance and lumbar hypolordosis, L₅-S₁ should be included in the fusion even if there was minimal degeneration of the L₅/S₁ disc. Elsayaf *et al.* reported 20 patients who had undergone anterior cervical discectomy and fusion (ACDF) and had a mean follow-up of 28 months¹⁷. They believed that the compensatory increase in the sagittal range of movement (ROM) of adjacent segments had a direct impact on the pathogenesis of ASD at contiguous levels, especially in cases with pre-existing asymptomatic degenerative disc disease at these levels. If these preliminary results are confirmed by larger series, it would be reasonable to adopt total disc arthroplasty rather than fusion after cervical micro-discectomy in young selected patients with soft disc herniation. Thus, it is necessary for the surgeon to reconstruct a close-to-physical spine alignment as the same time as treating the original disorder.

Longer is not better! The saying may also be applied to the length of spinal fusion. Cadaveric studies have reported a positive correlation between fusion length and adverse adjacent segment forces, many researchers having demonstrated that adjacent disc pressures increase with the number of fused vertebrae^{18–24}. In addition, retrospective studies have implicated disruption of the posterior tension band as a risk factor for adjacent level instability. A single-level arthrodesis involving the fifth or sixth cervical vertebra and pre-existing radio-

graphic evidence of degeneration at adjacent levels appear to be the greatest risk factors for new disease. Surprisingly, one study found that the risk of new disease at an adjacent level was significantly lower following a multilevel, rather than a single-level, arthrodesis. The investigators suggested that this finding may have been due to the inclusion of at-risk motion segments in the index procedure¹³.

Another commonly mentioned factor is lateral bending and axial rotation. Reviewing 9-year follow-up data on the ProDisc first-generation implant, Huang *et al.* found that total disc replacement (TDR) patients with a small ROM had increased adjacent level degeneration and an inferior clinical outcome^{25,26}. Lateral bending and axial rotation may well be significant factors affecting outcome, but are difficult to measure because the rotations are of such small magnitude.

Also, the impact on ASD of age^{27–31}, female gender, postmenopausal status^{27,28}, obesity, and postoperative pelvic incidence and tilt are generally accepted. In addition, extra care in protecting the facet joint during insertion of the superior pedicle screw and the use of slightly flexible rods are also thought to be factors which contribute to the outcome³².

However, not all researchers believe that ASD is associated only with the fusion itself. Narrowing of disk spaces has been observed in 31% of subjects, usually occurring at levels proximal to the fusion. After PLIF, the incidence of adjacent disk narrowing was not significantly higher than that reported for degenerative changes in lumbar disks with aging³³.

The study by Penta *et al.* reported that degenerative changes following spinal fusion are not related to the length of fusion³⁴. From this, they suggested that degeneration following lumbar interbody fusion is determined more by the degenerative disease process than by the fusion itself. Seitsalo *et al.* evaluated 227 patients treated either conservatively or with segmental fusion for spondylolisthesis and also noted no marked difference between the two groups in ASD³⁵. The addition of rigid instrumentation as a risk factor for earlier development of ASD is also debatable. Wiltse *et al.* compared 51 patients who underwent pedicle screw and rod augmented fusions with a similar control group of 31 patients who underwent uninstrumented fusions³¹. Surprisingly, a decreased incidence of ASD was observed in the instrumented group.

Besides, there is a 3-fold increase in risk of developing adjacent level disc degeneration in incorrectly marked discs after ACDF at one short-term follow-up. This may indicate that either needle related trauma or unnecessary surgical dissection contributes to accelerated adjacent segment degeneration³⁶.

Thus this remains a problem deserving further research. This article leans towards accepting that ASD results from a combination of spinal fusion and normal aging.

Biomechanics

An increase in adjacent intradisc pressure after fusion has been proved by some biomechanical tests in human cadaveric vertebrae by Weinholder *et al.*²² In response to destabilization and instrumentation, proximal disc pressures increased by as much as 45% in lumbar spines³⁴. The more levels involved in the simulated fusion, the more the intradiscal pressure increased²². Similar results were obtained for the cervical spine by Eck *et al.*, who found that significant increases in intradisc pressure and segmental mobility occur at levels adjacent to fusion during normal ROM³⁷. The rigidity of the interbody graft is also associated with increased internal stresses at adjacent discs.

Adjacent level degeneration is thought to result primarily from increased movement and stress of the adjacent segment, which may damage the annulus fibrosus and the vertebral end-plate³⁸. In addition, the fixed sagittal alignment of fused segments cannot accommodate the regional alignment changes that occur in sitting, supine, and erect postures.

Progress of ASD after lumbar fusion was explored in the animal study of Phillips *et al.*³⁹ Loss of the normal parallel arrangement of collagen bundles within the annular lamellae was observed in intervertebral discs adjacent to the fusion at three months. By six months there was further disorganisation as well as loss of distinction between the lamellae themselves. By nine months the structure of the disc had been replaced by disorganised fibrous tissue, and annular tears were seen. There was an initial cellular proliferative response followed by loss of chondrocytes and notochordal cells in the nucleus pulposus.

Prevention and treatment

The surgical prevention and treatment of ASD is a complicated and controversial topic for which there is no established guideline. Obviously, the primary target of surgeons is to maximize recovery of normal sagittal alignment and mobility. Most researchers now pay a lot of attention to the fusion length and whether or not to fuse.

Some authors have suggested that prevention of further degeneration and post-fusion pain may be achieved by fusion of the adjacent degenerated segments. However, others think it unnecessary to do that. In a retrospective review of 25 consecutive patients who underwent lumbar fusion for degenerative instability, Throckmorton *et al.*

found no adverse impact on clinical outcome when the fusion ended adjacent to a degenerative motion segment⁴⁰. Furthermore, long fusion length has been believed to be one of the primary risk factors for adjacent segment degeneration. Recently, another point of view which is accepted by many researchers is that prophylactic fusion of the adjacent segment may be beneficial in those patients with sagittal malalignment, instability, or overwhelming axial pain. Thus elimination of painful disc disease with restoration of sagittal alignment seems to play an important role in averting adjacent level degeneration, as well as being vital to a successful surgical outcome. There are, however, some authors who believe that adjacent segment degeneration is more a progression of the disease rather than a result of the fusion itself³.

It has generally been confirmed that fusion leads to a greater incidence of adjacent segment degeneration and disease, at least in short-term studies^{41–43}. Up to now, cervical disc arthroplasty has to some extent been as effective as cervical fusion in providing symptomatic relief while reducing perioperative morbidity, eliminating the need for postoperative external immobilization, and allowing for earlier return to normal function in certain cases⁴⁴. However, some researchers consider the degenerative process may be accelerated in patients with a cervical prosthesis, because the properties of this device remain unchanged as the patient's cervical spine ages and becomes more rigid⁴⁵. Anyway, long-term follow-up should be conducted in the future to assess the effect of non-fusion techniques.

Conclusion

ASD following spinal fusion is most likely to be a combined effect of several postoperative mechanical factors and the normal aging process of the spine. This review supports a multi-factor theory. The incidence of ASD is actually not very high. Different ways of treating the initial disease lead to different results. Even though an excellent short-term outcome can be achieved, non-fusion techniques, which are represented by artificial disc replacement and dynamic stabilization, should be adopted with caution until more long-term researchers report satisfactory results.

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References

1. Albee FH. Transplantation of a portion of the tibia into the spine for Pott's disease. *JAMA*, 1911, 57: 885–886.

2. Hibbs RA. An operation for progressive spinal deformities. *NY Med J*, 1911, 93: 1013.
3. Yoon ST, Howard SA. Cervical degenerative disc disease. In: Vaccaro AR, Betz RR, Zeidman SM, eds. *Principles and Practice of Spine Surgery*. Philadelphia: Mosby, 2003; 319.
4. Bohlman HH, Emery SE, Goodfellow DB, *et al.* Robinson anterior cervical discectomy and arthrodesis for cervical radiculopathy. Long-term follow-up of one hundred and twenty-two patients. *J Bone Joint Surg Am*, 1993, 75: 1298–1307.
5. Robinson RA, Smith GW. Anterolateral cervical disc removal and interbody fusion for cervical disc syndrome. *Bull Johns Hopkins Hosp*, 1955, 96: 223–224.
6. Okuda S, Iwasaki M, Miyauchi A, *et al.* Risk factors for adjacent segment degeneration after PLIF. *Spine*, 2004, 29: 1535–1540.
7. Xia LZ, Xu HG. Progress of adjacent segment degeneration after cervical surgery. *Guoji Gu Ke Xue Za Zhi*, 2007, 28: 258–260.
8. Matsumoto M, Nojiri K, Chiba K, *et al.* Open-door laminoplasty for cervical myelopathy resulting from adjacent-segment disease in patients with previous anterior cervical decompression and fusion. *Spine*, 2006, 31: 1332–1337.
9. Hilibrand AS, Robbins M. Adjacent segment degeneration and adjacent segment disease: the consequences of spinal fusion? *Spine J*, 2004, 4 (6 Suppl.): S190–S194.
10. Surawala SJ, Pinto MR, Gilbert TJ, *et al.* Functional and radiological outcomes of 360 degrees fusion of three or more motion levels in the lumbar spine for degenerative disc disease. *Spine*, 2009, 34: E351–E358.
11. Ghiselli G, Wang JC, Bhatia NN, *et al.* Adjacent segment degeneration in the lumbar spine. *J Bone Joint Surg Am*, 2004, 86: 1497–1503.
12. Katsuura A, Hukuda S, Saruhashi Y, *et al.* Kyphotic malalignment after anterior cervical fusion is one of the factors promoting the degenerative process in adjacent intervertebral levels. *Eur Spine J*, 2001, 10: 320–324.
13. Hilibrand AS, Carlson GD, Palumbo MA, *et al.* Radiculopathy and myelopathy at segments adjacent to the site of a previous anterior cervical arthrodesis. *J Bone Joint Surg Am*, 1999, 81: 519–528.
14. Levin DA, Hale JJ, Bendo JA, *et al.* Adjacent segment degeneration following spinal fusion for degenerative disc disease. *Bull NYU Hosp Jt Dis*, 2007, 65: 29–36.
15. Chen WJ, Lai PL, Tai CL, *et al.* The effect of sagittal alignment on adjacent joint mobility after lumbar instrumentation—a biomechanical study of lumbar vertebrae in a porcine model. *Clin Biomech (Bristol, Avon)*, 2004, 19: 763–768.
16. Cho KJ, Suk SI, Park SR, *et al.* Arthrodesis to L5 versus S1 in long instrumentation and fusion for degenerative lumbar scoliosis. *Eur Spine J*, 2009, 18: 531–537.
17. Elsawaf A, Mastronardi L, Roberto R, *et al.* Effect of cervical dynamics on adjacent segment degeneration after anterior cervical fusion with cages. *Neurosurg Rev*, 2009, 32: 215–224.
18. Cheh G, Bridwell KH, Lenke LG, *et al.* Adjacent segment disease following lumbar/thoracolumbar fusion with pedicle screw instrumentation: a minimum 5-year follow-up. *Spine*, 2007, 32: 2253–2257.
19. Panjabi MM. Biomechanical testing to quantify adjacent-level effects. *Proceeding of Trans IV World Congress of Biomechanics*. Calgary, Canada, 2002.
20. Lee CK, Langrana NA. Lumbosacral spinal fusion. A biomechanical study. *Spine*, 1984, 9: 574–581.
21. Shono Y, Kaneda K, Abumi K, *et al.* Stability of posterior spinal instrumentation and its effects on adjacent motion segments in the lumbosacral spine. *Spine*, 1998, 23: 1550–1558.
22. Weinholder SL, Guyer RD, Herbert M, *et al.* Intradiscal pressure measurements above an instrumented fusion. A cadaveric study. *Spine*, 1995, 20: 526–531.
23. Lai PL, Chen LH, Niu CC, *et al.* Relation between laminectomy and development of adjacent segment instability after lumbar fusion with pedicle fixation. *Spine*, 2004, 29: 2527–2532.
24. Papagelopoulos PJ, Peterson HA, Ebersold MJ, *et al.* Spinal column deformity and instability after lumbar or thoracolumbar laminectomy for intraspinal tumors in children and young adults. *Spine*, 1997, 22: 442–451.
25. Huang RC, Girardi FP, Cammisa FP Jr, *et al.* Long-term flexion-extension range of motion of the prodisc total disc replacement. *J Spinal Disord Tech*, 2003, 16: 435–440.
26. Huang RC, Girardi FP, Cammisa FP Jr, *et al.* The relationship between range of motion and outcome in lumbar total disc replacement at 9-year follow-up. *Proceeding of the International Society for the Study of the Lumbar Spine 31st Annual Meeting*. Porto, Portugal, 2004.
27. Etebar S, Cahill DW. Risk factors for adjacent-segment failure following lumbar fixation with rigid instrumentation for degenerative instability. *J Neurosurg*, 1999, 90: 163–169.
28. Aota Y, Kumano K, Hirabayashi S. Postfusion instability at the adjacent segments after rigid pedicle screw fixation for degenerative lumbar spinal disorders. *J Spinal Disord*, 1995, 8: 464–473.
29. Rahm MD, Hall BB. Adjacent-segment degeneration after lumbar fusion with instrumentation: a retrospective study. *J Spinal Disord*, 1996, 9: 392–400.
30. Kumar MN, Baklanov A, Chopin D. Correlation between sagittal plane changes and adjacent segment

- degeneration following lumbar spine fusion. *Eur Spine J*, 2001, 10: 314–319.
31. Wiltse LL, Radecki SE, Biel HM, *et al.* Comparative study of the incidence and severity of degenerative change in the transition zones after instrumented versus noninstrumented fusions of the lumbar spine. *J Spinal Disord*, 1999, 12: 27–33.
 32. Park P, Garton HJ, Gala VC, *et al.* Adjacent segment disease after lumbar or lumbosacral fusion: review of the literature. *Spine*, 2004, 29: 1938–1944.
 33. Nakai S, Yoshizawa H, Kobayashi S, *et al.* Long-term follow-up study of posterior lumbar interbody fusion. *J Spinal Disord*, 1999, 12: 293–299.
 34. Penta M, Sandhu A, Fraser RD. Magnetic resonance imaging assessment of disc degeneration 10 years after anterior lumbar interbody fusion. *Spine*, 1995, 20: 743–747.
 35. Seitsalo S, Schlenzka D, Poussa M, *et al.* Disc degeneration in young patients with isthmic spondylolisthesis treated operatively or conservatively: a long-term follow-up. *Eur Spine J*, 1997, 6: 393–397.
 36. Nassr A, Lee JY, Bashir RS, *et al.* Does incorrect level needle localization during anterior cervical discectomy and fusion lead to accelerated disc degeneration? *Spine*, 2009, 34: 189–192.
 37. Eck JC, Humphreys SC, Lim TH, *et al.* Biomechanical study on the effect of cervical spine fusion on adjacent level intradiscal pressure and segmental motion. *Spine*, 2002, 27: 2431–2434.
 38. Goto K, Tajima N, Chosa E, *et al.* Effects of lumbar spinal fusion on the other lumbar intervertebral levels (three-dimensional finite element analysis). *J Orthop Sci*, 2003, 8: 577–584.
 39. Phillips FM, Reuben J, Wetzel FT, *et al.* Intervertebral disc degeneration adjacent to a lumbar fusion. An experimental rabbit model. *J Bone Joint Surg Br*, 2002, 84: 289–294.
 40. Throckmorton TW, Hilibrand AS, Mencia GA, *et al.* The impact of adjacent level disc degeneration on health status outcomes following lumbar fusion. *Spine*, 2003, 28: 2546–2550.
 41. Robertson JT, Papadopoulos SM, Traynelis VC, *et al.* Assessment of adjacent-segment disease in patients treated with cervical fusion or arthroplasty: a prospective 2-year study. *J Neurosurg Spine*, 2005, 3: 417–423.
 42. Shin DA, Yi S, Yoon H, *et al.* Artificial disc replacement combined with fusion versus two-level fusion in cervical two-level disc disease. *Spine*, 2009, 34: 1153–1159.
 43. Highsmith JM, Tumialán LM, Rodts GE Jr, *et al.* Flexible rods and the case for dynamic stabilization. *Neurosurg Focus*, 2007, 22: E11.
 44. Acosta FL Jr, Ames CP. Cervical disc arthroplasty: general introduction. *Neurosurg Clin N Am*, 2005, 16: 603–607.
 45. Azmi H, Schlenk RP. Surgery for postarthrodesis adjacent-cervical segment degeneration. *Neurosurg Focus*, 2003, 15: E6.