Supplemental digital Material

Level of evidence (LoE) summary table for prognosis of development of ASD due to postsurgical malalignment in the cervical spine.

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| **Methodological principle** | **Faldini (2011)** | **Ishihara (2004)** | **Katsuura (2001)** | **Kulkarni (2004)** | **Matsumoto (2010)** |
| Study design |  |  |  |  |  |
| Prospective cohort study |  |  |  |  |  |
| Retrospective cohort study | + | + | + | + | + |
| Case-control study |  |  |  |  |  |
| Cross-sectional study |  |  |  |  |  |
| Case-series |  |  |  |  |  |
| **COHORT STUDIES** |  |  |  |  |  |
| Patients at similar point in the course of their disease or treatment | + | + | + | + | + |
| Complete follow-up of > 80% |  |  |  |  |  |
| Patients followed long enough for outcomes to occur | + | + | + | + | + |
| Accounting for other prognostic factors\* |  |  |  |  |  |
| **CASE-CONTROL STUDIES** |  |  |  |  |  |
| Incidence cases from defined population over a specified time period |  |  |  |  |  |
| Controls represent the population from which the cases come |  |  |  |  |  |
| Exposure precedes an outcome of interest |  |  |  |  |  |
| Accounting for other prognostic factors |  |  |  |  |  |
| **CROSS-SECTIONAL STUDIES** |  |  |  |  |  |
| A representative sample of the population of interest |  |  |  |  |  |
| Exposure that precedes an outcome of interest (e.g., sex, genetic factor) |  |  |  |  |  |
| Accounting for other prognostic factors |  |  |  |  |  |
| For surveys, a return rate of > 80% |  |  |  |  |  |
| **Evidence class** | **III** | **III** | **III** | **III** | **III** |

**Overall body of evidence summary.**

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| Baseline quality: HIGH = majority of article Level I/II. LOW = majority of articles Level III/IV.  UPGRADE: Large magnitude of effect (1 or 2 levels); dose response gradient (1 level)  DOWNGRADE: Inconsistency of results (1 or 2 levels); indirectness of evidence (1 or 2 levels); imprecision of effect estimates (1 or 2 levels) | | | | | |
|  | **Strength of evidence** | **Conclusions/Comments** | **Baseline** | **UPGRADE (levels)** | **DOWN-GRADE**  **(levels)** |
| Question: Does the presence or magnitude of postsurgical malalignment in the coronal (scoliosis) or sagittal plane (kyphosis/lordosis) affect the risk of cervical ASD? | | | | | |
| Sagittal malalignment | LOW | Limited data from 3 LoE III retrospective cohorts suggests that risk of ASD may be increased when malalignment occurs post-operatively | LOW | no | no |
| Coronal malalignment | INSUFFICIENT | No studies found | Insufficient | na | na |

**Detailed demographic and results table:**

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| **Study** | **Demographics** | **Inclusion/exclusion** | **How ASD defined and classified** | **Follow-up** | **Alignment groups** | **ASD outcomes** |
| Faldini (2011)  (retrospective cohort) | N = 107  Male = NR  Age = 35-55 years | Inclusion: One level cervical disc disease between C4-C7  Discectomy and single level anterior cervical fusion by Cloward procedure  Exclusion: NR | Standard radiographs; parameters of Kellgren and Lawrence:  grade 0 definite absence of degenerative changes  grade 1 doubtful presence of degeneration  grade 2 degeneration present but of minimal severity  grade 3 moderate degeneration  grade 4 severe degeneration | Mean 16 years (10-23); minimum 10 years | Sagittal segmental alignment (SSA)  Preoperative: 0.6° ±2.0°  Postoperative: 1.9° ± 4.2°  Last f/u: 1.8° ± 4.1°  (postop to last f/u; P = 0.861)  **Group A (SSA ≤0°):** n = 41 (mean -3.0° ± 1.2° postop)  **Group B (SSA >0°):** n = 66  (mean 5.0° ± 1.9° postop)  Mean sagittal alignment of cervical spine (SACS):  Preoperative: 17.0° ± 4.9°  Postoperative: 21.0° ± 6.2°  Last f/u: 19.7° ± 6.6°  (postop to last f/u; P = 0.639)  Cutoff value of 2° | % pts with ASD  Last f/u:  Whole series: 40%  Group A: 61%  Group B: 27%  OR 2.236; P < 0.001  Postop:  OR = 0.788 (95% CI, 0.708-0.877, P < 0.001)  Increase of postop SSA correlated with ASD; r = -0.428, P < 0.001  Increase of SSA at last f/u correlated with ASD; r =-0.432; P < .001  No correlation between postop SACS and ASD, or between last f/u SACS and ASD  Grade of ASD by group:  Grade 0: n = 7 group A; n = 29 group B  Grade 1: n = 9 group A; n = 19 group B  Grade 2: n = 14 group A; n = 15 group B  Grade 3: n = 8 group A; n = 3 group B  Grade 4: n = 3 group A; n = 0 group B  ASD rate by fusion level for n = 107 patients  C4-5 (n = 46): group A n = 11/20 (n = 55%); group B n = 9/26 (35%)  C5-6 (n = 34): group A n = 8/11 (73%); group B n = 5/23 (22%)  C6-7 (n = 27): group A n = 6/10 (60%); group B n = 4/17 (23.5%) |
| Ishihara (2004)  (retrospective cohort) | N = 112  Male: 66%  Mean age: 51 years (31-70) | Inclusions:  Intervertebral disc herniation and cervical spondylosis  Anterior cervical discectomy and arthrodesis using autogeneous iliac-crest graft without plate fixation; one level fusion n = 66, two level fusion n = 44, three level fusion n = 2  Exclusions: NR | Presence of both new radiculopathy or myelopathy symptoms referable to the adjacent level on MRI or myelography; evaluated by criteria of Hilibrand et al: intervertebral disc narrowing of > 2 mm compared with adjacent segments, osteophyte formation of > 2 mm, anterior or posterior slip of > 2 mm | Mean 9.4 years (2-19) | Lordosis or kyphosis preoperatively or postoperatively after fusion | ASD at f/u: n = 19 of 112 (17%)  No ASD  N = 93 of 112 (83%)  Preop alignment (+ is lordosis, - is kyphosis)  ASD: 11.4° ± 10.3°  No ASD: 7.7 ° ± 11.0°  P = 0.262  Fusion alignment (+ is lordosis, - is kyphosis)  ASD: 1.27° ± 2.82°  No ASD: -1.00° ± 6.78°  P = 0.217 |
| Katsuura (2001)  (retrospective cohort) | N = 42  Male: 81%  Age: 50.2 years (SD 9.4)  Degenerated adjacent level n= 21  Normal adjacent level n = 21 | Inclusions:  Anterior cervical fusion, no instrumentation, for degenerative disorders, cervical spondylosis or cervical disc herniation  Single level n = 23  Two level n = 17  Three level n = 2  Exclusions: NR | At least one of the following criteria met in comparison with preoperative radiographic findings:   * evident intervertebral disc space narrowing, * newly developed instability >3mm on flexion-extension radiographs, * vertebral posterior spur formation | Mean 9.8 years (5-22) | Alignment:  Lordotic n = 27  Straight n = 3  Kyphotic n = 8  Sigmoid n = 4  Alignment of the whole cervical spine = angle A  Alignment of the fused segment = angle B | Physiological cervical lordosis preserved in n = 18 (85.7%) in group with normal adjacent levels and in n = 9 (42.8%) in group with ASD (P = 0.0148)  Angle A both at preop and at f/u were significantly smaller in the ASD group than in the normal group (Table 3)  Angle B was not significantly different between groups preoperatively (P = ns) and was significantly smaller in the ASD group at f/u compared with the normal group (P = 0.0096) (Table 3) |
| Kulkarni (2004)  (retrospective cohort) | N = 44  Male: 98%  Mean age: 46 years (31-66) | Inclusions:  Central cervical corpectomy and fusion; one level n = 11; two level n = 33  Exclusions: NR | MRI evaluation of adjacent segments for indentation of the thecal sac, disc height, sagittal functional diameter of the spinal canal | Mean : 1.5 years (0.8-4) | Sagittal alignment:  Kyphotic alteration (lordotic spine became kyphotic or straight; straight spine became kyphotic) in n = 17  Preoperative alignment maintained or improved in n = 27 | ASD changes present:  Kyphotic alteration group: n = 15/17 (88%)  Alignment maintained: n = 18/27 (67%)  P = 0.1  (trend but not significant, as noted in conclusion of study) |
| Matsumoto (2010)  (retrospective cohort) | ACDF group:  N = 64  Male: 75%  Mean age 47.3 years  Asymptomatic group:  N = 201 | Inclusions:  One or two level noninstrumented ACDF for disc hernia or spondylosis  Preop MRI  No history of previous surgery  Exclusions:  Revision surgery for ASD after index surgery | MRI evaluation for degenerative findings; grading system used to evaluate:   * decrease in signal intensity of intervertebral disc * posterior disc protrusion * disc space narrowing * foraminal stenosis (evaluated on right and left sides) | Mean 12.1 years | Fusion in kyphosis:  **Group A, kyphosis angle ≥5°:** n = 23  **Group B, kyphosis angle <5°:** n = 41 | Degenerative MRI findings:  Decrease in signal intensity:  group A 60.9%, n = 14;  group B 53.7% n = 22  Posterior disc protrusion:  group A 65.2% n = 15; group B 78.0% n = 32  Disc space narrowing: group A 26.1% (n = 6); group B 19.5% (n = 8)  Foraminal stenosis: group A 26.1% (n = 6); group B 19.5% (n = 8)  (statistical eval not included in table or text) |

Search strategy

A search was made in PubMed for any articles pertaining to the topic of malalignment and adjacent segment disease or adjacent segment degeneration after fusion of the cervical spine; key words were used to find all articles which were concerned with ASD in the cervical spine; and then to determine which of those were also concerned with malalignment or alignment in kyphosis or lordosis. Articles which were biomechanical, or not human subjects, or not in English, were discarded; further articles were sought from bibliographies or pertinent articles and from Pubmed’s Related Articles feature. The title and abstract of 365 articles from the search were examined for possible relevance to the topic as outlined in the PPO table.

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| Search **#6 AND #7 AND (alignment OR kyphosis OR lordosis)** | [30](http://www.ncbi.nlm.nih.gov/pubmed/?cmd=HistorySearch&querykey=11) |
| Search **#6 AND #7** | [144](http://www.ncbi.nlm.nih.gov/pubmed/?cmd=HistorySearch&querykey=8) |
| Search **cervical spine AND (fusion OR arthroplasty OR arthrodesis OR ACDF OR disc replacement)** | [6186](http://www.ncbi.nlm.nih.gov/pubmed/?cmd=HistorySearch&querykey=7) |
| Search **"adjacent segment disease" OR "adjacent segment breakdown" OR "adjacent segment degeneration" OR "adjacent segment biomechanical consequences" OR "adjacent level degeneration" OR “adjacent level disease”** | [395](http://www.ncbi.nlm.nih.gov/pubmed/?cmd=HistorySearch&querykey=6) |

List of studies excluded at full text

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| Study | Reason for exclusion |
| Sekhon, L. H. (2003). "Cervical arthroplasty in the management of spondylotic myelopathy." J Spinal Disord Tech 16(4): 307-313. | Too short f/u for ASD results |
| Joo, Y. H., J. W. Lee, et al. (2010). "Comparison of fusion with cage alone and plate instrumentation in two-level cervical degenerative disease." J Korean Neurosurg Soc 48(4): 342-346. | Doesn’t connect kyphosis to ASD |
| Yue, W. M., W. Brodner, et al. (2005). "Long-term results after anterior cervical discectomy and fusion with allograft and plating: a 5- to 11-year radiologic and clinical follow-up study." Spine (Phila Pa 1976) 30(19): 2138-2144. | Does not connect alignment to ASD |
| Robertson, J. T., S. M. Papadopoulos, et al. (2005). "Assessment of adjacent-segment disease in patients treated with cervical fusion or arthroplasty: a prospective 2-year study." J Neurosurg Spine 3(6): 417-423. | Does not connect alignment to ASD |
| Kim, C. H., C. K. Chung, et al. (2011). "Comparisons of outcomes after single or multilevel dynamic stabilization: effects on adjacent segment." J Spinal Disord Tech 24(1): 60-67. | Doesn’t evaluate alignment as risk factor for ASD although mentions in discussion |
| Komura, S., K. Miyamoto, et al. (2012). "Lower Incidence of Adjacent Segment Degeneration After Anterior Cervical Fusion Found With Those Fusing C5-6 and C6-7 Than Those Leaving C5-6 or C6-7 as an Adjacent Level." J Spinal Disord Tech 25(1): 23-29. | Does not evaluate alignment as risk factors for ASD |
| Marotta, N., A. Landi, et al. (2011). "Five-year outcome of stand-alone fusion using carbon cages in cervical disc arthrosis." Eur Spine J 20 Suppl 1: S8-12. | Does not link malalignment to ASD |
| Ozer, E., K. Yucesoy, et al. (2007). "Kyphosis one level above the cervical disc disease: is the kyphosis cause or effect?" J Spinal Disord Tech 20(1): 14-19. | Does not link to ASD; analyzes KOLA |
| Coric, D., P. D. Nunley, et al. (2011). "Prospective, randomized, multicenter study of cervical arthroplasty: 269 patients from the Kineflex|C artificial disc investigational device exemption study with a minimum 2-year follow-up: clinical article." J Neurosurg Spine 15(4): 348-358. | No subanalysis of ASD risk factors including alignment |
| Maldonado, C. V., R. D. Paz, et al. (2011). "Adjacent-level degeneration after cervical disc arthroplasty versus fusion." Eur Spine J 20 Suppl 3: 403-407. | Does not evaluate sagittal angulation as a risk factor for ASD |
| Yoshida, G., M. Kamiya, et al. (2010). "Subaxial sagittal alignment and adjacent-segment degeneration after atlantoaxial fixation performed using C-1 lateral mass and C-2 pedicle screws or transarticular screws." J Neurosurg Spine 13(4): 443-450. | Did not link alignment to ASD |
| Beaurain, J., P. Bernard, et al. (2009). "Intermediate clinical and radiological results of cervical TDR (Mobi-C) with up to 2 years of follow-up." Eur Spine J 18(6): 841-850. | Did not link alignment to ASD |
| Kim, H. K., M. H. Kim, et al. (2009). "Surgical outcome of cervical arthroplasty using bryan(r)." J Korean Neurosurg Soc 46(6): 532-537. | No connection to ASD apparent |
| Koller, H., J. Reynolds, et al. (2009). "Mid- to long-term outcome of instrumented anterior cervical fusion for subaxial injuries." Eur Spine J 18(5): 630-653. | Didn’t analyze for connection of alignment to ASD |
| Kim, S. W., M. A. Limson, et al. (2009). "Comparison of radiographic changes after ACDF versus Bryan disc arthroplasty in single and bi-level cases." Eur Spine J 18(2): 218-231. | Postulates connection to ASD but did not analyze it. |
| Acikbas, S. C., C. Ermol, et al. (2010). "Assessment of adjacent segment degeneration in and between patients treated with anterior or posterior cervical simple discectomy." Turk Neurosurg 20(3): 334-340. | Not usable info for this topic |
| Barsa, P. and P. Suchomel (2007). "Factors affecting sagittal malalignment due to cage subsidence in standalone cage assisted anterior cervical fusion." Eur Spine J 16(9): 1395-1400. | Evaluates risk factors for cage subsidence and resultant malalignment |
| Elsawaf, A., L. Mastronardi, et al. (2009). "Effect of cervical dynamics on adjacent segment degeneration after anterior cervical fusion with cages." Neurosurg Rev 32(2): 215-224; discussion 224. | no eval of alignment as risk factor for ASD |
| Yoshida, G., M. Kamiya, et al. (2010). "Subaxial sagittal alignment and adjacent-segment degeneration after atlantoaxial fixation performed using C-1 lateral mass and C-2 pedicle screws or transarticular screws." J Neurosurg Spine 13(4): 443-450. | has some pediatric; doesn't give usable ASD info |
| Baba, H., N. Furusawa, et al. (1993). "Late radiographic findings after anterior cervical fusion for spondylotic myeloradiculopathy." Spine (Phila Pa 1976) 18(15): 2167-2173. | no data provided specific to ASD |
| Gore, D. R. and S. B. Sepic (1984). "Anterior cervical fusion for degenerated or protruded discs. A review of one hundred forty-six patients." Spine (Phila Pa 1976) 9(7): 667-671. | doesn't actually provide info upon examination of the paper, perhaps more background |
| Miyazaki, M., H. J. Hymanson, et al. (2008). "Kinematic analysis of the relationship between sagittal alignment and disc degeneration in the cervical spine." Spine (Phila Pa 1976) 33(23): E870-876. | not surgical |

**Discussion of the reliability results for methods for the determination of sagittal alignment in the cervical spine:**

The reliability study by Harrison et al (2000) determined standard errors of measurement (SEM) for intraobserver and interobserver correlation coefficients, for the Cobb method and the Harrison Posterior Tangent method (equivalent to Sagittal tangent method / ARA C2-C7; ARA = absolute rotation angle). This study determined that both methods were reliable with a majority of correlation coefficients in the high range (ICC > 0.7). The Cobb C1-C7 method overestimated cervical lordosis, and the Cobb C2-C7 angle underestimated lordosis, whereas the posterior tangent method ARA C2-C7 gave exact slopes of cervical curvature at each vertebra. The Cobb C1-C7 method gave an interclass CC (with 95% CI) of 0.91 (0.85-0.95) and intraclass CC of 0.94 (0.89-0.97). The Cobb C2-C7 method gave an interclass CC of 0.92 (0.87-0.96) and intraclass CC of 0.95 (0.92-0.98). The ARA C2-C7 method gave an interclass CC of 0.94 (0.90-0.97) and intraclass CC of 0.97 (0.95-0.99).