Demographic, Surgical, and Radiographic Risk Factors for Symptomatic Adjacent Segment Disease After Lumbar Fusion

A Systematic Review and Meta-Analysis

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Background: Although multiple studies have investigated risk factors for symptomatic adjacent segment disease (ASD) after lumbar fusion, their findings were diverse and inconsistent. This review aimed to summarize risk factors for ASD in order to guide the management of ASD and future research.

Methods: Six electronic databases were systematically searched from inception to December 2019. Two reviewers independently screened titles, abstracts, and full-text articles to identify studies investigating risk factors for ASD after lumbar fusion in humans. The methodological quality of the included studies and the strength of evidence regarding risk factors were evaluated.

Results: Sixteen studies involving 3,553 patients were included. Meta-analyses revealed that high body mass index, facet joint violation, anterior shift of the preoperative and postoperative lumbosacral sagittal plumb line, decreased preoperative and postoperative lumbar lordosis, preoperative adjacent disc degeneration, decreased preoperative adjacent disc height, increased postoperative lumbopelvic mismatch, postoperative pelvic incidence, and postoperative pelvic tilt were significantly related to ASD.

Conclusions: This meta-analysis addressed the limitations of prior reviews and summarized evidence with regard to risk factors for ASD following lumbar fusion. Future prospective studies should investigate whether modification of these risk factors can reduce the ASD development.

Level of Evidence: Prognostic Level IV. See Instructions for Authors for a complete description of levels of evidence.

Lumbar fusion is one of the most common surgical procedures for lumbar degenerative diseases, involving stabilization of spinal segments using bone graft after decompression of the spinal canal or foramina[1]. In the United States, the annual number of lumbar fusions increased by 262% from 1998 to 2015[2,3], and the incidence of lumbar fusions for lumbar disc degeneration also increased by 136% from 7.5 per 100,000 procedures in 2000 to 18.1 per 100,000 procedures in 2009[4]. Given the growing number of lumbar fusions, the relevant medical cost surged by 177% from $3.7 billion in 2004 to $10.2 billion in 2015[3]. Importantly, up to 20% of these cases needed reoperation within 4 years[5], placing heavy burdens on patients and the medical system.

Symptomatic adjacent segment disease (ASD) is a late complication of lumbar fusion that occurs adjacent to previously fused segments and is characterized by radiographic changes and associated symptoms[6]. Although the pathophysiology of disc degeneration is multifactorial[7], lumbar fusion may undoubtedly accelerate the process of adjacent segment degeneration[8]. Meta-regression analyses revealed that the pooled annual incidence rates were 6% for adjacent segment degeneration and 2% for ASD[9]. Because spinal decompression usually involves the removal of structures that may destabilize the spine[10], lumbar fusion is used to stabilize the decompressed segments at the expense of increased stress[11], shearing force[12], and mobility at intervertebral discs[13] or segments adjacent to the fused construct[14].

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Therefore, it is not uncommon to find post-fusion pathological changes (e.g., spondylolisthesis, segmental instability, stenosis, disc herniation, and scoliosis) in adjacent segments, leading to back symptoms[15].

Because ASD is the major cause of revision surgical procedures after lumbar fusion[5], several reviews have attempted to investigate risk factors for ASD in order to develop proper prevention strategies[16-20]. However, because prior reviews had some limitations (e.g., selective reporting, or inclusion of studies with unclear preoperative adjacent segment degeneration), their findings were diverse and inconsistent. Additionally, many recent studies continued to investigate the same topic without addressing the limitations of prior research. Therefore, this review aimed to summarize the risk factors for ASD after lumbar fusion so as to inform or update busy clinicians with regard to clinical decision-making and researchers with regard to future research directions.

Materials and Methods

The current review was conducted according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines. The study protocol was registered at the PROSPERO (International Prospective Register of Systematic Reviews) database (CRD42019141107).

Search Strategy

Six databases (Academic Search Premier, CINAHL, CENTRAL, Embase, MEDLINE, and Web of Science [WoS]) were searched from inception to December 18, 2019. Search strings involved 4 sets of keywords: lumbar spine, fusion surgery, adjacent segment disease, and risk factors (Appendix 1). There was no language restriction during the search. Additional relevant publications were identified by forward citation searching via Scopus and contacting the corresponding authors of all included studies.

Study Selection

Primary studies, regardless of study design, were eligible for inclusion if they involved patients who underwent lumbar fusion, determination of risk factors for ASD (including preoperative adjacent segment degeneration), and statistical analysis (e.g., odds ratio [OR] and/or mean difference [MD]) of risk factors for ASD. Notably, because the presence of preoperative degeneration of adjacent discs and/or facets might affect the postoperative condition of adjacent discs or facets[8], only studies that assessed these factors were included. Cadaveric studies, case reports, commentaries, reviews, conference proceedings, study protocols, or non-English articles were excluded. After the removal of duplicates, 2 independent reviewers (K.K.L.L. and N.S.C.T.) conducted the title-abstract screening and then the full-text screening based on the selection criteria. Disagreements were resolved by discussion between 2 reviewers at both screening stages. Further disagreements were resolved with a third reviewer (A.Y.L.W.). Additionally, ASD was operationally defined as the symptomatic degeneration of segments adjacent to the operated vertebral levels with or without reoperation[6], and diagnosed by both radiographic signs and clinical symptoms. The definitions of ASD in all included studies were scrutinized by the 2 reviewers (K.K.L.L. and A.Y.L.W.) to confirm the appropriateness for inclusion.

Data Extraction and Quality Assessments

Information related to the methodology, participants, index surgery, ASD, and risk factors for ASD was extracted. Study-reported estimates related to the associations between various risk factors and ASD (e.g., OR), or the MD of parameters between patients with and without ASD, were extracted. Because all of the identified studies had either a retrospective cohort or a case-control design, the risk of bias was assessed by the respective Newcastle-Ottawa Scale (NOS) for cohort and case-control studies[21], which are validated tools for these study designs[22]. A maximum of 9 points could be given to a given study. A study was rated as having a low risk of bias if the NOS score was ≥7, a high risk of bias if the NOS score was between 4 and 6, and a very high risk of bias if the NOS score was ≤3[23]. Two reviewers (K.K.L.L. and N.S.C.T.) independently extracted data and performed the methodological quality assessment of each included study, although they were not blinded to the authors or institutions. The third reviewer (A.Y.L.W.) was consulted for unsolved disagreements.

Strength of Evidence

Each risk factor was evaluated qualitatively on the basis of the consistency of statistical findings for a given risk factor and the methodological quality of the relevant included studies[24]. The strength of evidence of each risk factor was categorized as strong, moderate, limited, very limited, conflicting, or no evidence (see Appendix 2).

Statistical Analysis

The principal summary measure was the OR for dichotomous data and the MD for continuous data. The corresponding 95% conference intervals (CIs) were reported. Risk factors for ASD were compared between patients with and without ASD. Common risk factors identified from the included studies were pooled for meta-analyses. Random-effects models were used to analyze all pooled risk factors. The homogeneity among studies was evaluated by the I^2 statistic. RevMan 5.4 (Cochrane Training) was used for the meta-analyses. Significance was set at $p < 0.05$. Publication bias was evaluated by funnel plots if there were >10 studies in a given meta-analysis[25].

Results

Search Outcomes

The literature search retrieved 1,307 records (see Appendix 3). No additional studies were identified through other sources. After duplicate removal, 665 records were screened on the basis of the titles and abstracts. Of 63 articles that then underwent full-text screening, 47 were excluded for unclear information with regard to preoperative adjacent disc or segment degeneration (n = 27), including a mixed group of patients with asymptomatic adjacent segment degeneration and ASD (n = 8), not mentioning ASD (n = 7), or not involving

lumbar fusion (n = 4) or the lumbar spine (n = 1). Therefore, 16 studies with 3,553 patients were included in the current review[26-41].

Study Characteristics

The characteristics of the included studies are shown in Table I. All included studies adopted retrospective designs (11 cohort and 5 case-control studies). These studies were published between 2004 and 2019 from 6 countries: Japan (n = 5); South Korea (n = 5); People's Republic of China (n = 3); and 1 each from Iran, Switzerland, and the United States. Their sample sizes ranged from 40 to 630, with a mean of 222 participants. The mean follow-up duration was 49.8 months, and the median of the minimum follow-up period was 2 years. Surgical procedures included posterior, posterolateral, and transforaminal lumbar fusion. Although definitions of ASD were similar across studies, no standardized radiographic and clinical criteria were used in diagnosing ASD. Eleven included studies showed that all of their patients with ASD underwent reoperation. Two studies documented that a proportion of patients with ASD required reoperation. Three studies did not mention whether their patients with ASD underwent reoperation. The mean occurrence rate (and standard deviation) of ASD among the included studies was 13.4% ± 5.5%, and the mean ASD-related reoperation rate was 11.2% ± 7.4%. One study was classified as having a low risk of bias, 11 studies had a high risk of bias, and 4 studies had a very high risk of bias (see Appendix 4).

Data Synthesis

The included studies identified 21 demographic, 8 surgical, and 49 radiographic risk factors for ASD. All significant risk factors for ASD are presented in Table II, and all nonsignificant risk factors for ASD are presented in Appendix 5. Twenty-two meta-analyses were performed to summarize common risk factors identified from the included studies (Figs. 1 to 3; see also Appendix 6); 11 of them were significant. Only 1 meta-analysis involved enough studies (11) for funnel plot analysis, which showed no publication bias (see Appendix 7). Given the numerous investigated risk factors, only those significant risk factors with moderate-quality evidence (defined in Appendix 2) were reported and discussed.

Demographic and Surgical Risk Factors

A meta-analysis of 3 studies indicated that patients with ASD had a higher body mass index (BMI) than patients without ASD (438 patients; pooled MD, 2.77 kg/m^2 [95% CI, 1.68 to 3.85 kg/m^2]; $p < 0.00001$; $I^2 = 54\%$) (Fig. 1). Similarly, a meta-analysis of 2 studies suggested that perioperative facet joint violation heightened the risk of ASD development (867 patients; pooled OR, 30.30 [95% CI, 17.62 to 52.10]; $p < 0.00001$; $I^2 = 0\%$) (Fig. 1, Table II).

Radiographic Risk Factors

There was moderate-quality evidence that patients with ASD were characterized by significantly smaller preoperative adjacent disc height (4 studies; 395 patients; pooled MD, −0.69 mm [95% CI, −1.26 to −0.11 mm]; $p = 0.02$; $I^2 = 19\%$), greater preoperative anterior shift of the lumbosacral sagittal plumb line (4 studies; 952 patients; pooled MD, 7.01 mm [95% CI, 4.96 to 9.06 mm]; $p < 0.00001$; $I^2 = 0\%$), and smaller preoperative lumbar lordosis (11 studies; 2,014 patients; pooled MD, −4.19° [95% CI, −6.66° to −1.71°]; $p < 0.00001$; $I^2 = 76\%$) than patients without ASD (Fig. 2, Table II). Furthermore, the presence of preoperative adjacent disc degeneration with a Pfirrmann grade of ≥3 doubled the risk of developing ASD (8 studies; 1,877 patients; pooled OR, 1.91 [95% CI, 1.19 to 3.06]; $p < 0.01$; $I^2 = 60\%$) (Fig. 2, Table II).

Compared with patients without ASD, patients with ASD were characterized by significantly greater postoperative anterior shift of the lumbosacral sagittal plumb line (4 studies; 952 patients; pooled MD, 3.98 mm [95% CI, 2.46 to 5.49 mm]; $p < 0.001$; $I^2 = 0\%$), smaller postoperative lumbar lordosis (9 studies; 1,639 patients; pooled MD, −5.50° [95% CI, −7.59° to −3.40°]; $p < 0.001$; $I^2 = 37\%$), greater postoperative lumbopelvic mismatch (2 studies; 231 patients; pooled MD, 4.56° [95% CI, 0.95° to 8.17°]; $p = 0.01$; $I^2 = 0\%$), larger postoperative pelvic incidence (4 studies; 475 patients; pooled MD, 3.69° [95% CI, 0.67° to 6.71°]; $p = 0.02$; $I^2 = 38\%$), and larger postoperative pelvic tilt (5 studies; 507 patients; pooled MD, 3.20° [95% CI, 1.68° to 4.71°]; $p < 0.001$; $I^2 = 0\%$) (Fig. 3, Table II).

Discussion

Our meta-analyses addressed the limitations of prior reviews to comprehensively summarize risk factors for ASD after lumbar fusion. Moderate-quality evidence supported 11 significant demographic (n = 1), preoperative (n = 4), perioperative (n = 1), and postoperative (n = 5) risk factors for ASD between 29 and 77 months postoperatively.

High BMI was the only demographic risk factor for ASD. Overweight and obesity increase the mechanical loading of intervertebral discs and affect the shock-absorbing properties of discs[42], which may increase the loading of surrounding facet joints and spinal ligaments[43].

Surgeons should explain the risk of ASD to overweight or obese patients based on ethnicity-specific BMI cutoffs and should refer them to weight management programs before and/or after the surgical procedure to lower their risk of developing ASD.

Facet joint violation, defined as a screw within 1 mm of a facet joint, is a perioperative risk factor for ASD[44]. Because the facet joint and intervertebral discs are spinal stabilization structures, facet joint violation may cause sagittal instability and accelerated degeneration[45]. Because the risk of facet joint violation during pedicle screw insertion is related to surgeons' experience[29], junior surgeons or residents should conduct such a procedure with or without robot-guided screw placement under supervision[46]. Given the high OR of this risk factor, further investigation is warranted.

Although a prior meta-analysis found that a longer fusion length increased the risk of an ASD-related reoperation[20], our review found inconsistent evidence with regard to the relation between the fusion length and ASD. The discrepancy might be ascribed to different outcomes of interest and the exclusion of

TABLE I Characteristics of the Included Studies*

Included Study	Country	Sample Size	Age† *(yr)*	Sex	Follow-up† *(mo)*	Diagnosis for Index Fusion	Type(s) of Index Fusion	Definition of ASD	Occurrence Rate of ASD	Revision Surgery
Retrospective cohort study										
Bagheri[28] (2019)	Iran	630 total (76 ASD, 554 control)	61.4 ASD, 62.4 control	M: 303, F: 327	51 ASD, 52 control	Degenerative lumbar disorders including degenerative spondylolisthesis, spinal stenosis, disc herniation, degenerative scoliosis	Posterior transpedicular lumbar instrumentation	"The pathological process at the closest disc space to the previously fused levels leading to clinical symptoms including radiculopathy, stenosis, and instability."	12.1%	NA
Wang[29] (2017)	People's Republic of China	237 total (15 ASD, 222 control)	55.3 ASD, 53.1 control	M: 106, F: 131	31 ASD, 30 control	Degenerative lumbar disorders	Posterior lumbar interbody fusion, transforaminal lumbar interbody fusion	"The pathologic process associated with disc degeneration leading to clinical symptoms, such as radiculopathy, stenosis, and instability."	6.3%	NA
Wang[30] (2017)	People's Republic of China	117 total (21 ASD, 96 control)	56.4 ASD, 54.6 control	M: 57, F: 60	42 ASD, 41 control	Lumbar spinal stenosis, lumbar disc herniation and instability, lumbar spondylolisthesis	Posterior lumbar interbody fusion	"Fusion-related symptoms like lower back pain or radicular symptoms followed by the degeneration of adjacent segment when other causes were excluded."	18.0%	NA
Zhong[31] (2017)	United States	154 total (18 ASD, 136 control)	59.8 ASD, 58.2 control	M: 44, F: 110	29 overall	Spondylolisthesis	Instrumented fusion	"A condition in which a patient showed the relief of symptoms for at least 3 months after the index operation, the development of new clinical symptoms was compatible with radiographic changes at adjacent segments, and the patient needed second surgery for this problem."	11.7%	100%
Yugué[32] (2016)	Japan	161 total (44 ASD, 117 control)	65.4 overall	M: 56, F: 105	77 overall	Degenerative spondylolisthesis	Instrumented posterolateral fusion, posterior lumbar interbody fusion	"A condition where an additional surgery at L3-4 was required to treat symptomatic neurological deterioration."	27.3%	100%
Heo[33] (2015)	South Korea	378 total (33 ASD, 345 control)	62.8 ASD, 58.7 control	M: 125, F: 253	72 overall	Spondylolisthesis	Posterior lumbar interbody fusion, posterolateral fusion	"Received fusion extension surgery at the L3-4 level because of low back pain with radiological instability, radiculopathy, or claudication due to degenerative pathology at the L3-4 disc level, was unresponsive to medication or pain block, and had a prior history of L4-5 or L4/5-S1 fusion."	8.7%	100%
Lee[34] (2015)	South Korea	115 total (16 ASD, 99 control)	58.2 overall	M: 44, F: 71	46 overall	Spinal stenosis, spondylolisthesis, degenerative scoliosis	Transforaminal lumbar interbody fusion	"1. Newly developed back pain and/or radiculopathy in relation to the adjacent operation sites 2. Newly developed lesions in the adjacent segments of patients who did not have radiographic and/or clinical changes within 6 months postoperatively"	13.9%	6.09%
Cho[36] (2014)	South Korea	154 total (10 ASD, 144 control)	64.5 ASD, 58.8 control	M: 49, F: 105	30 overall	Degenerative conditions refractory to conservative treatment	Posterior lumbar interbody fusion	"Required a second operation because of stenosis, disc herniation, spondylolisthesis, retrolisthesis, and intractable back pain and neurologic deterioration."	6.5%	100%
Sakaura[38] (2013)	Japan	40 total (4 ASD, 36 control)	53.5 ASD, 59.1 control	M: 26, F: 14	67 overall	Isthmic spondylolisthesis	Posterior lumbar interbody fusion	"Newly developed or aggravated neurologic symptoms due to adjacent segment pathology"	10.0%	100%

continued

TABLE I (*continued*)

Included Study	Country	Sample Size	Age† *(yr)*	Sex	Follow-up† *(mo)*	Diagnosis for Index Fusion	Type(s) of Index Fusion	Definition of ASD	Occurrence Rate of ASD	Revision Surgery
Kaito[39] (2010)	Japan	85 total (13 ASD, 14 radiographic ASD, 58 control)	66.0 ASD, 63.4 control	M: 29, F: 56	37 ASD, 39 control	Spondylolisthesis	Posterior lumbar interbody fusion	"A decrease by 4 points or more on the scale of Japanese Orthopaedic Association scoring system accompanied by neurological impairment in accordance with adjacent canal stenosis."	15.3%	12.94%
Okuda[41] (2004)	Japan	87 total (4 ASD, 25 radiographic ASD, 58 control)	64.0 ASD, 64.0 control	M: 38, F: 49	43 overall	Radicular pain or neuralgic claudication (or both) resistant to conservative treatment	Posterior or posterolateral fusion, posterior lumbar interbody fusion	"1. An additional surgery required for neurologic deterioration 2. Postoperative progression of adjacent segment degeneration in which narrowing of disc height was greater than 3 mm, posterior opening was greater than 5°, and progress of slippage was greater than 3 mm in comparison with preoperative flexion and extension lateral radiographs"	4.6%	100%
Retrospective case-control study										
Kim[27] (2019)	South Korea	77 total (37 ASD, 40 control)	69.6 ASD, 65.6 control	M: 30, F: 47	72 ASD, 77 control	Degenerative lumbar disorders with leg pain and claudication	Posterior or Posterolateral instrumented fusion	"When spinal canal stenosis and disk herniation were observed at the adjacent segment on MRI and underwent revision surgery for at least 3 months in which symptoms persisted."	NA	100%
Matsumoto[28] (2017)	Japan	120 total (20 ASD, 100 control)	68.9 ASD, 66.7 control	M: 49, F: 71	37 ASD, 68 control	Degenerative spondylolisthesis, lumbar foraminal stenosis, lumbar disc herniation	Posterior lumbar interbody fusion	"A condition in which additional surgery was required to treat neurological deterioration."	NA	100%
Rothenfluh[35] (2015)	Switzerland	84 total (45 ASD, 39 control)	58.0 ASD, 64.0 control	M: 33, F: 51	71 overall	Degenerative lumbar spondylosis or spondylolisthesis with leg pain or claudication	Posterolateral instrumented fusion	"Patients underwent primary lumbar fusion of 1, 2, or 3 segments between L2 and S1 and had surgery for symptomatic adjacent segment."	NA	100%
Liang[37] (2014)	People's Republic of China	84 total (28 ASD, 56 control)	61.4 ASD, 62.1 control	M: 29, F: 55	NA	Degenerative lumbar disease (back pain symptoms attributable to intervertebral disc degeneration that includes pathologic changes in the disc, annulus, and the end plates, with or without osteophyte formation at the vertebral apophyses)	Posterior lumbar fusion	"Degeneration at a segment adjacent to a fusion-causing symptom."	NA	100%
Lee[40] (2009)	South Korea	52 total (26 ASD, 26 control)	58.4 ASD, 58.2 control	NA	NA	Degenerative conditions	Instrumented lumbar fusion	"A condition in which a patient showed the relief of symptoms for at least 6 months after the index operation, the newly developed symptoms were compatible with the lesions in adjacent segments demonstrated in radiological images, and the patient had revision surgery for that problem."	NA	100%

*NA = not available, and MRI = magnetic resonance imaging. †The values are given as the mean.

TABLE II Common and Significant Risk Factors for ASD from Individual Studies*

Risk Factor	Study	No. of Patients	Statistics	ASD Group†	Control Group†	Results†	P Value
Demographic							
Increased body mass index§ *(kg/m²)*	Bagheri[26] (2019)	76 ASD, 554 control	Independent t test	27.9; SD not reported	23.2; SD not reported	MD, 4.7#	0.033#
	Wang[29] (2017)**	15 ASD, 222 control	Independent t test	27.7 ± 2.0	24.1 ± 1.8	MD, 3.6 (2.7 to 4.6)	<0.001
	Wang[30] (2017)**	21 ASD, 96 control	Independent t test	25.2 ± 3.5	23.6 ± 3.5	MD, 1.6 (−0.1 to 3.3)	0.060
	Zhong[31] (2017)	18 ASD, 136 control	Chi-square test	>25 kg/m²: 7, ≤25 kg/m²: 11	>25 kg/m²: 47, ≤25 kg/m²: 89	OR, 1.2 (0.4 to 3.3)	0.718
	Yugué[32] (2016)	44 ASD, 117 control	Log-rank test	NA	NA	HR, 3.1# (1.2 to 8.5)	0.021#
	Cho[36] (2014)	10 ASD, 144 control	Independent t test	26.8; SD not reported	24.3; SD not reported	MD, 2.5#	0.02#
	Liang[37] (2014)**	28 ASD, 56 control	Independent t test	27.9 ± 2.3	25.2 ± 3.3	MD, 2.7 (1.3 to 4.1)	<0.001
Surgical							
Facet joint violation††	Bagheri[26] (2019)**	76 ASD, 554 control	Chi-square test	Yes: 55, no: 21	Yes: 41, no: 513	OR, 32.8 (18.1 to 59.4)	<0.001
	Wang[29] (2017)**	15 ASD, 222 control	Chi-square test	Yes: 12, no: 3	Yes: 36, no: 186	OR, 20.7 (5.6 to 76.9)	<0.001
Adjacent segment decompression†‡	Zhong[31] (2017)	18 ASD, 136 control	Chi-square test	Yes: 7, no: 11	Yes: 16, no: 120	OR, 4.8 (1.6 to 14.1)	0.005
Radiographic							
Preoperative measures							
Anterior shift distance of the L1-to-S1 sagittal plumb line§§ *(mm)*	Bagheri[26] (2019)**	76 ASD, 554 control	Independent t test	22.15 ± 9.2	15.35 ± 8.1	MD, 6.8 (4.8 to 8.8)	<0.001
	Zhong[31] (2017)	18 ASD, 136 control	Independent t test	29.8 ± 21.9	22.2 ± 24.8	MD, 7.8 (−4.5 to 19.7)	0.218
	Rothenfluh[35] (2015)**	45 ASD, 39 control	Mann-Whitney U test	42.7 ± 76.1	21.0 ± 82.4	MD, 21.7 (−12.7 to 56.1)	0.213
	Liang[37] (2014)**	28 ASD, 56 control	Independent t test	22.8 ± 16.5	14.2 ± 17.0	MD, 8.6 (0.9 to 16.4)	0.030
Lumbar lordosis## *(deg)*	Bagheri[26] (2019)**	76 ASD, 554 control	Independent t test	32.34 ± 12.1	40.41 ± 0.3	MD, −8.1 (−9.1 to −7.1)	<0.001
	Kim[27] (2019)**	37 ASD, 40 control	Independent t test	40.6 ± 9.5	41.8 ± 10.1	MD, −1.2 (−5.7 to 3.3)	0.594
	Matsumoto[28] (2017)**	20 ASD, 100 control	Independent t test	40.7 ± 9.6	47.2 ± 10.2	MD, −6.5 (−11.4 to −1.6)	0.010
	Wang[29] (2017)**	15 ASD, 222 control	Independent t test	24.2 ± 2.0	24.7 ± 1.9	MD, −0.5 (−1.5 to 0.5)	0.327
	Wang[30] (2017)**	21 ASD, 96 control	Independent t test	41.6 ± 8.5	42.8 ± 9.0	MD, −1.13 (−5.38 to 3.12)	0.599
	Zhong[31] (2017)**	18 ASD, 136 control	Independent t test	56.9 ± 11.4	57.4 ± 13.3	MD, −0.5 (−7.0 to 6.0)	0.879
	Heo[33] (2015)**	33 ASD, 345 control	Independent t test	40.7 ± 12.7	46.5 ± 14.4	MD, −5.8 (−10.9 to −0.7)	0.026
	Rothenfluh[35] (2015)**	45 ASD, 39 control	Independent t test	48.8 ± 13.5	54.6 ± 9.6	MD, −5.8 (−11.0 to −0.6)	0.028
	Cho[36] (2014)	10 ASD, 144 control	Independent t test	32.5; SD not reported	38.6; SD not reported	NA	0.110#
	Liang[37] (2014)**	28 ASD, 56 control	Independent t test	34.4 ± 14.4	43.0 ± 12.2	MD, −8.6 (−14.6 to −2.6)	0.005
	Kaito[39] (2010)**	13 ASD, 58 control	Independent t test	33.4 ± 10.3	36.5 ± 10.9	MD, −3.1 (−9.7 to 3.5)	0.353
	Okuda[41] (2004)**	4 ASD, 58 control	Independent t test	35 ± 15	47 ± 10	MD, −12.0 (−22.7 to −1.3)	0.028
Adjacent disc degeneration cephalic and caudal to the index fusion*** *(Pfirrmann grade)*	Bagheri[26] (2019)**	76 ASD, 554 control	Chi-square test	≥3: 47, <3: 29	≥3: 173, <3: 381	OR, 3.6 (2.2 to 5.9)	<0.001
	Kim[27] (2019)**	37 ASD, 40 control	Chi-square test	≥3: 19, <3: 18	≥3: 22, <3: 18	OR, 0.9 (0.4 to 2.1)	0.749
	Wang[29] (2017)**	15 ASD, 222 control	Chi-square test	≥3: 8, <3: 7	≥3: 65, <3: 157	OR, 2.8 (1.0 to 7.9)	0.059
	Wang[30] (2017)**	21 ASD, 96 control	Chi-square test	≥3: 16, <3: 5	≥3: 78, <3: 18	OR, 0.7 (0.2 to 2.3)	0.598
	Zhong[31] (2017)**	18 ASD, 136 control	Chi-square test	≥3: 21, <3: 11	≥3: 116, <3: 122	OR, 2.0 (0.9 to 4.4)	0.077
	Heo[33] (2015)**	33 ASD, 345 control	Chi-square test	≥3: 27, <3: 6	≥3: 199, <3: 143, missing data: 3	OR, 3.2 (1.3 to 8.0)	0.012
	Lee[34] (2015)	16 ASD, 99 control	OR	NA	NA	OR, 5.1# (1.8 to 14.6)	0.002#
	Rothenfluh[35] (2015)**	45 ASD, 39 control	Chi-square test	≥3: 23, <3: 21, missing data: 1	≥3: 21, <3: 18	OR, 0.9 (0.4 to 2.2)	0.886
	Cho[36] (2014)	10 ASD, 144 control	Independent t test	3.9; SD not reported	3.1; SD not reported	MD, 0.8#	NS#
	Liang[37] (2014)**	28 ASD, 56 control	Chi-square test	≥3: 16, <3: 12	≥3: 16, <3: 40	OR, 3.3 (1.3 to 8.6)	0.013
	Lee[40] (2009)	26 ASD, 26 control	OR	NA	NA	OR, 0.5# (0.2 to 1.4)	0.17#
	Okuda[41] (2004)	4 ASD, 58 control	Independent t test	3.2 ± 0.5	3.1 ± 0.7	MD, 0.1 (−0.6 to 0.8)	0.781

continued

TABLE II (*continued*)

Risk Factor	Study	No. of Patients	Statistics	ASD Group†	Control Group†	Results†	P Value
Decreased adjacent disc height††† *(mm)*	Matsumoto[28] (2017)**	20 ASD, 100 control	Independent t test	(L3-L4) 8.0 ± 1.7	L3-L4: 8.5 ± 1.8	MD, −0.5 (−1.4 to 0.4)	0.255
	Matsumoto[28] (2017)**	20 ASD, 100 control	Independent t test	(L5-S1) 7.3 ± 2.4	L5-S1: 7.5 ± 2.2	MD, −0.2 (−1.3 to 0.9)	0.715
	Liang[37] (2014)**	28 ASD, 56 control	Independent t test	8.8 ± 2.5	10.4 ± 2.2	MD, −1.6 (−2.7 to −0.5)	0.004
	Kaito[39] (2010)**	13 ASD, 58 control	Mann-Whitney U test	9.5 ± 2.0	10.0 ± 1.8	MD, −0.5 (−1.6 to 0.6)	0.378
Lumbar disc bulge††	Liang[37] (2014)	28 ASD, 56 control	Fisher exact test	Yes: 27, no: 1	Yes: 8, no: 48	OR, 162.0 (19.2 to 1,365.5)	<0.001
Adjacent vertebral retrolisthesis†† *(mm)*	Kaito[39] (2010)	13 ASD, 58 control	Independent t test	1.6 ± 1.7	0.8 ± 1.1	MD, 0.8 (0.6 to 1.6)	0.037
Adjacent segment spinal stenosis†† *(%)*	Lee[34] (2015)	16 ASD, 99 control	Log-rank test	NA	NA	HR, 7.4# (2.0 to 36.3)	0.008#
	Cho[36] (2014)	10 ASD, 144 control	Chi-square test	Yes: 4, no: 6	Yes: 15, no: 129	OR, 5.7 (1.5 to 22.6)	0.013
Paraspinal muscle degeneration†† *(% fatty infiltration)*	Wang[29] (2017)	15 ASD, 222 control	Independent t test	15.1 ± 6.6	11.7 ± 7.3	MD, −6.6 (−10.4 to −2.8)	<0.001
Postoperative measures							
Anterior shift of the L1-to-S1 sagittal plumb line††† *(mm)*	Bagheri[26] (2019)**	76 ASD, 554 control	Independent t test	18.2 ± 6.8	14.3 ± 4.1	MD, 3.9 (2.8 to 5.0)	<0.001
	Zhong[31] (2017)**	18 ASD, 136 control	Independent t test	29.8 ± 21.9	22.2 ± 24.8	MD, 7.6 (−4.5 to 19.7)	0.218
	Rothenfluh[35] (2015)**	45 ASD, 39 control	Independent t test	39.4 ± 68.2	23.6 ± 61.4	MD, 15.8 (−12.6 to 44.2)	0.271
	Liang[37] (2014)**	28 ASD, 56 control	Independent t test	17.6 ± 18.1	14.5 ± 14.0	MD, 3.1 (−4.0 to 10.2)	0.389
Decreased lumbar lordosis§§§ *(deg)*	Bagheri[26] (2019)**	76 ASD, 554 control	Independent t test	31.4 ± 10.1	38.72 ± 2.3	MD, −7.37 (−8.4 to −6.4)	<0.001
	Kim[27] (2019)**	37 ASD, 40 control	Mann-Whitney U test	40.7 ± 11.8	45.2 ± 10.8	MD, −4.5 (−9.6 to 0.6)	0.085
	Matsumoto[28] (2017)**	20 ASD, 100 control	Independent t test	39.3 ± 13.5	48.1 ± 10.9	MD, −8.8 (−14.3 to −3.3)	0.002
	Wang[30] (2017)**	21 ASD, 96 control	Independent t test	35.1 ± 9.4	41.2 ± 7.9	MD, −6.2 (−10.0 to −2.3)	0.002
	Zhong[31] (2017)**	18 ASD, 136 control	Independent t test	56.6 ± 12.4	57.0 ± 13.3	MD, −0.4 (−6.9 to 6.1)	0.904
	Heo[33] (2015)**	33 ASD, 345 control	Mann-Whitney U test	40.7 ± 12.7	46.5 ± 14.4	MD, −5.8 (−10.9 to −0.7)	0.026
	Rothenfluh[35] (2015)**	45 ASD, 39 control	Independent t test	48.1 ± 12.5	53.8 ± 10.8	MD, −5.7 (−10.8 to −0.6)	0.029
	Liang[37] (2014)**	28 ASD, 56 control	Independent t test	33.3 ± 11.4	39.8 ± 10.4	MD, −6.5 (−10.6 to −2.4)	0.002
	Sakaura[38] (2013)**	4 ASD, 36 control	Mann-Whitney U test	46.8 ± 12.7	35.3 ± 11.0	MD, 11.5 (−0.4 to 23.4)	0.058
Greater lumbopelvic mismatch### *(deg)*	Kim[27] (2019)**	37 ASD, 40 control	Mann-Whitney U test	13.1 ± 13.4	7.3 ± 9.3	MD, 5.8 (0.6 to 11.0)	0.029
	Matsumoto[28] (2017)	20 ASD, 100 control	Chi-square test	>10°: 15, ≤10°: 5	>10°: 43, ≤10°: 57	OR, 3.98 (1.3 to 11.8)	0.013
	Zhong[31] (2017)**	18 ASD, 136 control	Independent t test	8.9 ± 9.7	5.5 ± 13.4	MD, 3.4 (−3.1 to 9.9)	0.300
Increased pelvic incidence**** *(deg)*	Matsumoto[28] (2017)**	20 ASD, 100 control	Independent t test	59.4 ± 8.4	57.3 ± 9.7	MD, 2.1 (−2.5 to 6.7)	0.369
	Wang[30] (2017)**	21 ASD, 96 control	Independent t test	55.1 ± 9.7	53.7 ± 11.0	MD, 1.4 (−3.7 to 6.6)	0.583
	Zhong[31] (2017)**	18 ASD, 136 control	Independent t test	65.6 ± 12.2	62.4 ± 15.1	MD, 3.2 (−4.1 to 10.5)	0.390
	Rothenfluh[35] (2015)**	45 ASD, 39 control	Independent t test	59.5 ± 10.1	51.7 ± 10.4	MD, 7.8 (3.3 to 12.3)	<0.001
Increased pelvic tilt†††† *(deg)*	Kim[27] (2019)**	37 ASD, 40 control	Mann-Whitney U test	22.3 ± 8.7	21.3 ± 7.7	MD, 1.0 (−2.7 to 4.7)	0.594
	Matsumoto[28] (2017)**	20 ASD, 100 control	Independent t test	26.4 ± 6.0	22.6 ± 7.8	MD, 3.8 (0.1 to 7.5)	0.042
	Wang[30] (2017)**	21 ASD, 96 control	Independent t test	20.9 ± 7.5	16.65 ± 5.6	MD, 4.2 (1.4 to 7.1)	0.004
	Zhong[31] (2017)**	18 ASD, 136 control	Independent t test	25.8 ± 7.2	23.1 ± 9.1	MD, 2.7 (−1.7 to 7.1)	0.229
	Rothenfluh[35] (2015)**	45 ASD, 39 control	Independent t test	22.4 ± 7.0	18.6 ± 6.5	MD, 3.8 (0.9 to 6.8)	0.012
Thoracic kyphosis†† *(deg)*	Matsumoto[28] (2017)	20 ASD, 100 control	Independent t test	22.5 ± 11.2	30.9 ± 10.3	MD, −8.4 (−13.47 to −3.33)	0.001

continued

TABLE II (*continued*)

Risk Factor	Study	No. of Patients	Statistics	ASD Group†	Control Group†	Results†	P Value
Decreased adjacent disc height†† *(mm)*	Liang[37] (2014)	28 ASD, 56 control	Independent t test	8.5 ± 2.4	10.1 ± 2.2	MD, −1.6 (−2.64 to −0.56)	0.003
Adjacent disc height difference†† *(mm)*	Heo[33] (2015)	33 ASD, 345 control	Independent t test	1.8 ± 2.7	2.8 ± 2.5	MD, −1.0 (−1.9 to −0.1)	0.035
Adjacent spinal stenosis on myelography††	Yugué[32] (2016)	44 ASD, 117 control	Log-rank test	NA	NA	HR, 4.9# (2.1 to 12.8)	<0.001#
Facet tropism†† *(deg)*	Yugué[32] (2016)	44 ASD, 117 control	Log-rank test	NA	NA	HR, 3.7# (1.4 to 10.3)	0.011#

*SD = standard deviation, NA = not available, and NS = not significant. †The values are either given as the mean and the standard deviation (if reported) or as the number of patients. ‡The values are given as the MD, OR, or hazard ratio (HR), with the 95% CI in parentheses. §The pooled MD was 2.8 (95% CI, 1.7 to 3.9; p < 0.001), and the quality of evidence was moderate. #This value was reported from the study. **These studies were included in the meta-analysis of a given risk factor. ††The pooled OR was 30.3 (95% CI, 17.6 to 52.1; p < 0.001), and the quality of evidence was moderate. ‡‡The quality of evidence was limited. §§The pooled MD was 7.0 (95% CI, 5.0 to 9.1; p < 0.001), and the quality of evidence was moderate. ##The pooled MD was −4.2 (95% CI, −6.7 to −1.7; p < 0.001), and the quality of evidence was moderate. ***The pooled OR was 1.91 (95% CI, 1.19 to 3.06; p = 0.007), and the quality of evidence was moderate. †††The pooled MD was −0.7 (95% CI, −1.3 to −0.1; p = 0.02), and the quality of evidence was moderate. ‡‡‡The pooled MD was 4.0 (95% CI, 2.5 to 5.5; p < 0.001), and the quality of evidence was moderate. §§§The pooled MD was −5.5 (95% CI, −7.6 to −3.4; p < 0.001), and the quality of evidence was moderate. ###The pooled MD was 4.6 (95% CI, 0.95 to 8.2; p = 0.01), and the quality of evidence was moderate. ****The pooled MD was 3.7 (95% CI, 0.67 to 6.7; p = 0.02), and the quality of evidence was moderate. ††††The pooled MD was 3.2 (95% CI, 1.7 to 4.7; p < 0.001), and the quality of evidence was moderate.

studies with unclear preoperative adjacent segment degeneration in our review. Because 1 of our included studies substantiated that patients with >4 levels of lumbar fusion were 4 times more likely to have ASD than those with fewer fusion levels[26], future research should determine whether a certain fusion length increases the risk of ASD.

Preoperative radiographic biomarkers help to identify patients at risk for developing ASD. A forward shift of the preoperative lumbosacral sagittal plumb line may indicate either an abnormal sagittal alignment (i.e., forward inclination) or poor pelvic compensation for a kyphotic spine[37]. The moment imposed by the center of mass on the lumbar spine should be counterbalanced by the moment created by paraspinal muscles to maintain an erect posture[47]. A more anteriorly shifted sagittal plumb line creates greater anterior and posterior moments about the lower lumbar spine, resulting in increased downward compressive force on the lumbar spine. If this is not corrected postoperatively, it can overload the unfused adjacent motion segments, resulting in ASD[37]. Similarly, smaller preoperative lumbar lordosis causes the gravity line to move forward and increases the contact force on the lumbar spine and discs[48,49] and has been suggested as a radiographic predictor for future clinical symptoms following a decompression surgical procedure[50]. Surgical restoration of appropriate lumbar lordosis (i.e., approximately 33°)[51] and correct regional alignment (i.e., a T1 pelvic angle of 10° to 25°)[52] may lower the risk of ASD development.

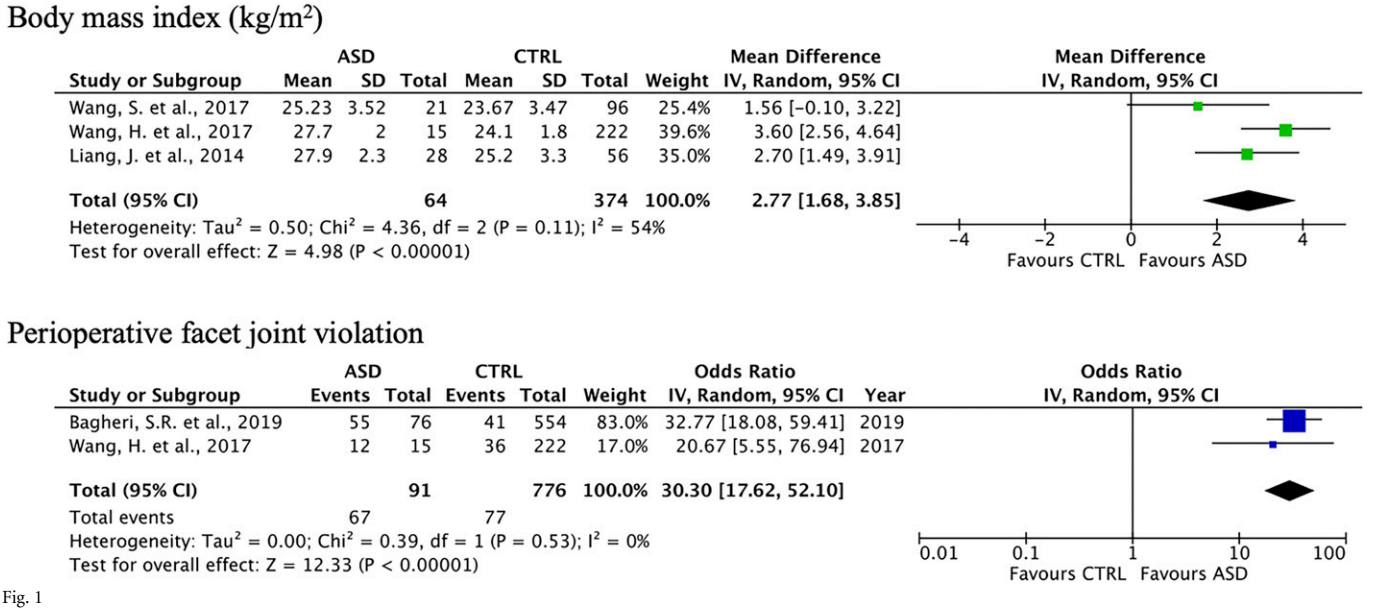


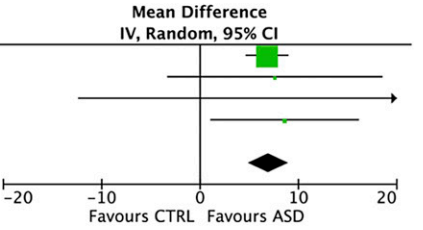
Fig. 1

Meta-analyses of common demographic and surgical risk factors for ASD compared with a control group without ASD (i.e., CTRL). SD = standard deviation, IV = inverse variance, and df = degrees of freedom.

Preoperative lumbosacral sagittal plumb line distance (mm)

Study or Subgroup	ASD Mean	ASD SD	ASD Total	CTRL Mean	CTRL SD	CTRL Total	Weight	Mean Difference IV, Random, 95% CI	Year
Bagheri, S.R. et al., 2019	22.15	9.2	76	15.35	8.1	554	88.8%	6.80 [4.62, 8.98]	2019
Zhong, Z.M. et al., 2017	29.8	21.9	18	22.2	24.8	136	3.5%	7.60 [-3.34, 18.54]	2017
Rothenfluh, D.A. et al., 2015	42.7	76.1	45	21	82.4	39	0.4%	21.70 [-12.41, 55.81]	2015
Liang, J. et al., 2014	22.8	16.5	28	14.2	17	56	7.3%	8.60 [1.04, 16.16]	2014
Total (95% CI)			**167**			**785**	**100.0%**	**7.01 [4.96, 9.06]**	

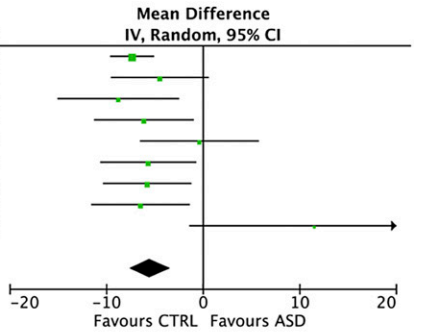
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.93$, df = 3 (P = 0.82); $I^2 = 0\%$
Test for overall effect: Z = 6.71 (P < 0.00001)



Preoperative lumbar lordosis (degrees)

Study or Subgroup	ASD Mean	ASD SD	ASD Total	CTRL Mean	CTRL SD	CTRL Total	Weight	Mean Difference IV, Random, 95% CI	Year
Bagheri, S.R. et al., 2019	31.35	10.1	76	38.72	2.3	554	23.4%	-7.37 [-9.65, -5.09]	2019
Kim, W.J. et al., 2019	40.7	11.8	37	45.2	10.8	40	11.2%	-4.50 [-9.57, 0.57]	2019
Matsumoto, T. et al., 2017	39.3	13.5	20	48.1	10.9	100	8.3%	-8.80 [-15.09, -2.51]	2017
Wang, S. et al., 2017	35.05	9.37	15	41.2	7.87	57	10.9%	-6.15 [-11.31, -0.99]	2017
Zhong, Z.M. et al., 2017	56.6	12.4	18	57	13.3	136	8.5%	-0.40 [-6.55, 5.75]	2017
Rothenfluh, D.A. et al., 2015	48.1	12.5	45	53.8	10.8	39	11.4%	-5.70 [-10.68, -0.72]	2015
Heo, Y. et al., 2015	40.67	12.67	33	46.48	14.35	345	12.7%	-5.81 [-10.39, -1.23]	2015
Liang, J. et al., 2014	33.3	11.4	28	39.8	11	56	11.1%	-6.50 [-11.61, -1.39]	2014
Sakaura, H. et al., 2013	46.8	12.7	4	35.3	11	36	2.4%	11.50 [-1.45, 24.45]	2013
Total (95% CI)			**276**			**1363**	**100.0%**	**-5.50 [-7.59, -3.40]**	

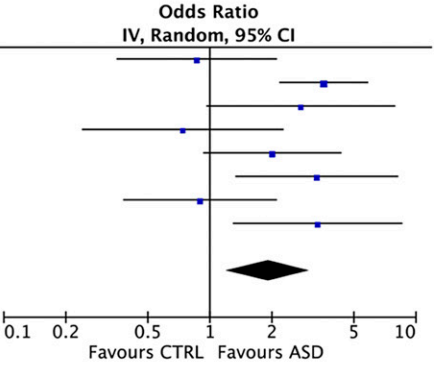
Heterogeneity: $Tau^2 = 3.53$; $Chi^2 = 12.74$, df = 8 (P = 0.12); $I^2 = 37\%$
Test for overall effect: Z = 5.14 (P < 0.00001)



Preoperative adjacent disc degeneration (Pfirrmann Grade ≥3)*

Study or Subgroup	ASD Events	ASD Total	CTRL Events	CTRL Total	Weight	Odds Ratio IV, Random, 95% CI	Year
Kim, W.J. et al., 2019	19	37	22	40	12.2%	0.86 [0.35, 2.12]	2019
Bagheri, S.R. et al., 2019	47	76	173	554	17.6%	3.57 [2.17, 5.86]	2019
Wang, H. et al., 2017	8	15	65	222	10.4%	2.76 [0.96, 7.93]	2017
Wang, S. et al., 2017	16	21	78	96	9.7%	0.74 [0.24, 2.28]	2017
Zhong, Z.M. et al., 2017	21	32	116	238	13.8%	2.01 [0.93, 4.35]	2017
Heo, Y. et al., 2015	27	33	199	345	12.0%	3.30 [1.33, 8.20]	2015
Rothenfluh, D.A. et al., 2015	23	45	21	39	12.7%	0.90 [0.38, 2.12]	2015
Liang, J. et al., 2014	16	28	16	56	11.6%	3.33 [1.29, 8.59]	2014
Total (95% CI)		**287**		**1590**	**100.0%**	**1.91 [1.19, 3.06]**	
Total events	177		690				

Heterogeneity: $Tau^2 = 0.26$; $Chi^2 = 17.34$, df = 7 (P = 0.02); $I^2 = 60\%$
Test for overall effect: Z = 2.69 (P = 0.007)



Preoperative adjacent disc height (mm)

Study or Subgroup	ASD Mean	ASD SD	ASD Total	CTRL Mean	CTRL SD	CTRL Total	Weight	Mean Difference IV, Random, 95% CI	Year
Matsumoto, T. et al., 2017	7.3	2.4	20	7.5	2.2	100	21.4%	-0.20 [-1.34, 0.94]	2017
Matsumoto, T. et al., 2017	8	1.7	20	8.5	1.8	100	35.5%	-0.50 [-1.32, 0.32]	2017
Liang, J. et al., 2014	8.8	2.5	28	10.4	2.2	56	23.0%	-1.60 [-2.69, -0.51]	2014
Kaito, T. et al., 2010	9.5	2	13	10	1.8	58	20.1%	-0.50 [-1.68, 0.68]	2010
Total (95% CI)			**81**			**314**	**100.0%**	**-0.69 [-1.26, -0.11]**	

Heterogeneity: $Tau^2 = 0.07$; $Chi^2 = 3.69$, df = 3 (P = 0.30); $I^2 = 19\%$
Test for overall effect: Z = 2.35 (P = 0.02)

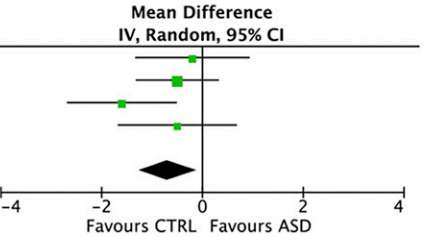


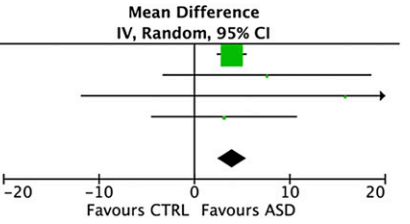
Fig. 2

Meta-analyses of common preoperative radiographic risk factors for ASD compared with a control group without ASD (i.e., CTRL). *Pfirrmann grade 3: inhomogeneous disc with an intermittent gray signal intensity, unclear distinction between nucleus and anulus, and normal or slightly decreased disc height. Grade 4: inhomogeneous disc with a hypointense dark gray signal intensity, no more distinction between the nucleus and anulus, slightly or moderately decreased disc height. Grade 5: inhomogeneous disc with a hypointense black signal intensity, no more difference between the nucleus and anulus, and a collapsed disc. SD = standard deviation, IV = inverse variance, and df = degrees of freedom.

Postoperative lumbosacral sagittal plumb line distance (mm)

Study or Subgroup	ASD Mean	ASD SD	ASD Total	CTRL Mean	CTRL SD	CTRL Total	Weight	Mean Difference IV, Random, 95% CI	Year
Bagheri, S.R. et al., 2019	18.24	6.8	76	14.34	4.1	554	93.8%	3.90 [2.33, 5.47]	2019
Zhong, Z.M. et al., 2017	29.8	21.9	18	22.2	24.8	136	1.9%	7.60 [−3.34, 18.54]	2017
Rothenfluh, D.A. et al., 2015	39.4	68.2	45	23.6	61.4	39	0.3%	15.80 [−11.92, 43.52]	2015
Liang, J. et al., 2014	17.6	18.1	28	14.5	14	56	3.9%	3.10 [−4.54, 10.74]	2014
Total (95% CI)			**167**			**785**	**100.0%**	**3.98 [2.46, 5.49]**	

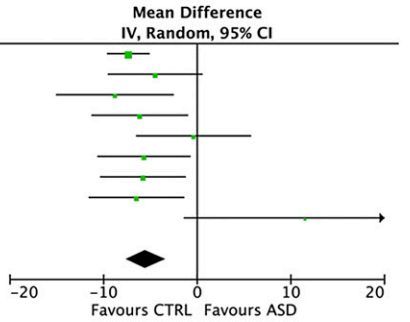
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.18$, df = 3 (P = 0.76); $I^2 = 0\%$
Test for overall effect: Z = 5.13 (P < 0.00001)



Postoperative lumbar lordosis (degrees)

Study or Subgroup	ASD Mean	ASD SD	ASD Total	CTRL Mean	CTRL SD	CTRL Total	Weight	Mean Difference IV, Random, 95% CI	Year
Bagheri, S.R. et al., 2019	31.35	10.1	76	38.72	2.3	554	23.4%	−7.37 [−9.65, −5.09]	2019
Kim, W.J. et al., 2019	40.7	11.8	37	45.2	10.8	40	11.2%	−4.50 [−9.57, 0.57]	2019
Matsumoto, T. et al., 2017	39.3	13.5	20	48.1	10.9	100	8.3%	−8.80 [−15.09, −2.51]	2017
Wang, S. et al., 2017	35.05	9.37	15	41.2	7.87	57	10.9%	−6.15 [−11.31, −0.99]	2017
Zhong, Z.M. et al., 2017	56.6	12.4	18	57	13.3	136	8.5%	−0.40 [−6.55, 5.75]	2017
Rothenfluh, D.A. et al., 2015	48.1	12.5	45	53.8	10.8	39	11.4%	−5.70 [−10.68, −0.72]	2015
Heo, Y. et al., 2015	40.67	12.67	33	46.48	14.35	345	12.7%	−5.81 [−10.39, −1.23]	2015
Liang, J. et al., 2014	33.3	11.4	28	39.8	11	56	11.1%	−6.50 [−11.61, −1.39]	2014
Sakaura, H. et al., 2013	46.8	12.7	4	35.3	11	36	2.4%	11.50 [−1.45, 24.45]	2013
Total (95% CI)			**276**			**1363**	**100.0%**	**−5.50 [−7.59, −3.40]**	

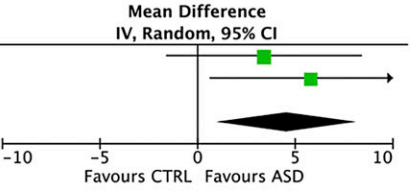
Heterogeneity: $Tau^2 = 3.53$; $Chi^2 = 12.74$, df = 8 (P = 0.12); $I^2 = 37\%$
Test for overall effect: Z = 5.14 (P < 0.00001)



Postoperative lumbopelvic mismatch (degrees)

Study or Subgroup	ASD Mean	ASD SD	ASD Total	CTRL Mean	CTRL SD	CTRL Total	Weight	Mean Difference IV, Random, 95% CI	Year
Zhong, Z.M. et al., 2017	8.9	9.7	18	5.5	13.4	136	51.7%	3.40 [−1.62, 8.42]	2017
Kim, W.J. et al., 2019	13.1	13.4	37	7.3	9.3	40	48.3%	5.80 [0.61, 10.99]	2019
Total (95% CI)			**55**			**176**	**100.0%**	**4.56 [0.95, 8.17]**	

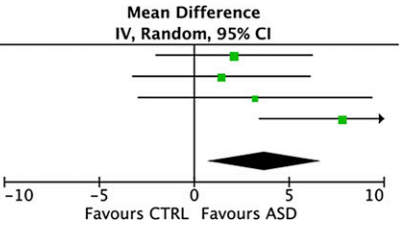
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.42$, df = 1 (P = 0.51); $I^2 = 0\%$
Test for overall effect: Z = 2.48 (P = 0.01)



Postoperative pelvic incidence (degrees)

Study or Subgroup	ASD Mean	ASD SD	ASD Total	CTRL Mean	CTRL SD	CTRL Total	Weight	Mean Difference IV, Random, 95% CI	Year
Matsumoto, T. et al., 2017	59.4	8.4	20	57.3	9.7	100	29.5%	2.10 [−2.04, 6.24]	2017
Wang, S. et al., 2017	55.14	9.72	21	53.71	11	96	25.4%	1.43 [−3.27, 6.13]	2017
Zhong, Z.M. et al., 2017	65.6	12.2	18	62.4	15.1	136	17.6%	3.20 [−2.98, 9.38]	2017
Rothenfluh, D.A. et al., 2015	59.5	10.1	45	51.7	10.4	39	27.5%	7.80 [3.40, 12.20]	2015
Total (95% CI)			**104**			**371**	**100.0%**	**3.69 [0.67, 6.71]**	

Heterogeneity: $Tau^2 = 3.58$; $Chi^2 = 4.83$, df = 3 (P = 0.18); $I^2 = 38\%$
Test for overall effect: Z = 2.40 (P = 0.02)



Postoperative pelvic tilt (degrees)

Study or Subgroup	ASD Mean	ASD SD	ASD Total	CTRL Mean	CTRL SD	CTRL Total	Weight	Mean Difference IV, Random, 95% CI	Year
Kim, W.J. et al., 2019	22.3	8.7	37	21.3	7.7	40	16.9%	1.00 [−2.68, 4.68]	2019
Matsumoto, T. et al., 2017	26.4	6	20	22.6	7.8	100	24.7%	3.80 [0.76, 6.84]	2017
Wang, S. et al., 2017	20.86	7.47	15	16.65	5.61	57	13.9%	4.21 [0.16, 8.26]	2017
Zhong, Z.M. et al., 2017	25.8	7.2	18	23.1	9.1	136	17.1%	2.70 [−0.96, 6.36]	2017
Rothenfluh, D.A. et al., 2015	22.4	7	45	18.6	6.5	39	27.4%	3.80 [0.91, 6.69]	2015
Total (95% CI)			**135**			**372**	**100.0%**	**3.20 [1.68, 4.71]**	

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.00$, df = 4 (P = 0.74); $I^2 = 0\%$
Test for overall effect: Z = 4.14 (P < 0.0001)

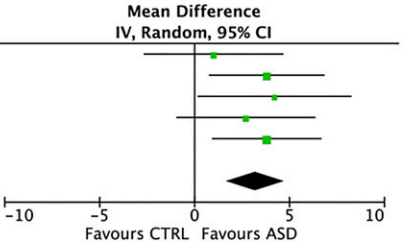


Fig. 3

Meta-analyses of common postoperative radiographic risk factors for ASD compared with a control group without ASD (i.e., CTRL). SD = standard deviation, IV = inverse variance, and df = degrees of freedom.

Preoperative adjacent disc degeneration increases the risk of ASD[8,29] because these degenerated discs need to withstand postoperative compensatory hypermobility adjacent to the fused construct[53]. Preoperative adjacent disc degeneration (i.e., decreased disc height[54] or Pfirrmann grade of ≥3)[55] can inform surgeons about patients' likelihood of developing ASD. Therefore, it is important to consider preoperative radiographic phenotypes during surgical planning[56,57]. Future studies should adjust for these confounders in evaluating the relative influences of other risk factors for ASD.

Unlike preoperative adjacent disc degeneration, preoperative adjacent facet degeneration showed conflicting relations with ASD. The discrepancy might be attributed to the fact that the Pfirrmann grading system for lumbar disc degeneration had higher intraobserver and interobserver reliability (kappa of 0.84 to 0.90 and 0.74 to 0.81, respectively) than the Weishaupt grading system for lumbar facet joint degeneration (kappa of 0.70 to 0.76 and 0.41, respectively)[58]. Future research should establish the reliability of these grading systems before use.

Postoperative spinopelvic sagittal alignment was significantly related to ASD. Reduced lumbar lordosis after a rigid nonphysiological kyphotic fusion may increase biomechanical stress on the spinal column (especially axial loading to discs) and causes hypermobility at the adjacent segment to compensate for the decreased motion of the fused segment[59], which accelerates the adjacent segment degeneration[60]. Decreased lumbar lordosis also causes compensatory increases in pelvic tilt (pelvic retroversion) to maintain sagittal balance[61]. However, if the increased pelvic tilt cannot restore the global spinal alignment, it may lead to poor clinical outcomes and quality of life[62]. The observation that patients with ASD displayed significantly larger pelvic tilt than patients without ASD might indicate that patients with ASD could not compensate for the decreased lumbar lordosis by simply increasing pelvic tilt. Therefore, both postoperative reduced lumbar lordosis and increased pelvic tilt are significant risk factors for ASD. Further, because large pelvic incidence requires more lumbar lordosis correction to restore proper sagittal balance[63], patients with large pelvic incidence are at risk for developing ASD.

The close association between spinopelvic sagittal parameters and ASD is further substantiated by the greater lumbopelvic mismatch in patients with ASD. Lumbopelvic mismatch (i.e., pelvic incidence minus lumbar lordosis) describes the difference between pelvic morphology and the lumbar curvature[35]. Patients with lumbopelvic mismatch of >15° have a higher risk of an ASD-related reoperation[35,64]. Because lumbopelvic mismatch of >10° indicates sagittal imbalance, larger lumbopelvic mismatch may predispose patients to develop ASD[64]. A threshold of lumbopelvic mismatch of ≤10° has been recommended as the surgical goal for spinopelvic sagittal alignment[65]; future research should evaluate whether the attainment of this threshold can reduce ASD development in the short and long terms[66].

The included studies had several limitations. First, because they excluded patients with <12-month follow-up, older or sicker patients may have been less likely to be included. Second, as some included studies were underpowered, they may have led to nonsignificant risk factors in individual studies or in our meta-analyses. Third, because most included studies reviewed medical records over a fixed period, the reasons for attrition, characteristics of the dropout individuals, and follow-up times were not documented, which may have affected the identified risk factors. Fourth, most of the included studies were conducted in Asia, so the results may not be generalizable to other races. Fifth, although the I^2 values for the meta-analyses of 8 significant common risk factors were <50% (indicating acceptable heterogeneity), 3 other meta-analyses had I^2 values of ≥50%, indicating substantial heterogeneity[61]. Such results should be interpreted with care. Sixth, this review only included English publications; however, only 2 potential non-English articles were identified in the screening process. Our results thus should have encompassed most of the risk factors for ASD. Seventh, the reviewers were not blinded to the authors and institutions during the risk-of-bias assessments, which might have caused assessment bias and might have affected the grading.

To enable the comparisons of results across future studies, an international consortium should be formed to determine a standard definition for ASD. Although our meta-analysis found some nonsignificant risk factors, the negative findings may have been attributable to the high heterogeneity of the included primary studies. Future research should verify our results by investigating risk factors with sound theoretical backgrounds or preliminary evidence (e.g., for paraspinal muscles)[67,68] and/or nonsignificant risk factors with large I^2 statistics in our meta-analyses.

Collectively, this meta-analysis addressed the limitations of previous reviews and meta-analyses and summarized evidence with regard to various risk factors for ASD following lumbar fusion. Although preoperative adjacent segment degeneration is nonmodifiable, it is plausible to lower the risk of ASD by modifying other risk factors (e.g., lumbopelvic mismatch). Future prospective research should determine the causal relationships between various factors and ASD, and evaluate the effects of modifying these factors on subsequent ASD development.

Appendix

eA Supporting material provided by the authors is posted with the online version of this article as a data supplement at jbjs.org (http://links.lww.com/JBJS/G579). ■

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