Evidence-Based Surgical Management of Spondylolisthesis: Reduction or Arthrodesis in Situ

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Background: The role of reduction in the operative management of spondylolisthesis is controversial because of its potential complications, including neurologic deficits, prolonged operative time, and loss of reduction. The aim of this systematic review was to compare arthrodesis in situ and arthrodesis after reduction techniques with respect to clinical and radiographic outcomes and safety.

Methods: We performed a comprehensive search of the PubMed, Ovid MEDLINE, Cochrane, CINAHL, Google Scholar, and Embase databases with use of the keyword ''spondylolisthesis'' in combination with ''surgery,'' ''reduction,'' ''in situ,'' ''low back pain,'' ''high-grade,'' ''lumbar spine,'' ''lumbar instability,'' and ''fusion.''

Results: Eight eligible studies, containing reports of 165 procedures involving reduction followed by arthrodesis and 101 procedures involving arthrodesis in situ without reduction, were identified and included. The procedure involving reduction was associated with a significantly greater decrease in the percentage of slippage ($p < 0.002$) and slip angle ($p < 0.003$) compared with arthrodesis in situ. Pseudarthrosis was significantly more frequent in the arthrodesis in situ group compared with the reduction group (17.8% compared with 5.5%, $p = 0.004$). Neurologic deficits were not significantly more prevalent in the reduction group compared with the arthrodesis in situ group (7.8% compared with 8.9%, $p = 0.8$).

Conclusions: On the basis on this review, the reduction of high-grade spondylolisthesis potentially improves overall spine biomechanics by correcting the local kyphotic deformity and reducing vertebral slippage. Reduction was not associated with a greater risk of developing neurologic deficits compared with arthrodesis in situ. Both procedures were associated with good clinical outcomes.

Level of Evidence: Therapeutic Level III. See Instructions for Authors for a complete description of levels of evidence.

Peer Review: This article was reviewed by the Editor-in-Chief and one Deputy Editor, and it underwent blinded review by two or more outside experts. It was also reviewed by an expert in methodology and statistics. The Deputy Editor reviewed each revision of the article, and it underwent a final review by the Editor-in-Chief prior to publication. Final corrections and clarifications occurred during one or more exchanges between the author(s) and copyeditors.

In spondylolisthesis, a vertebra (frequently in the lumbar spine) slips forward on the one below it[1-3]. Nonoperative management may lead to satisfactory results in many patients, but surgery is indicated for high-grade slippage in patients with persistent symptoms, including pain or neurologic impairment[4-7].

Typically, a minimum of three months of nonoperative management utilizing a brace, exercises, and a variety of other nonoperative modalities produces good results[4-10]. Surgical management should be considered when back and/or leg pain or neurogenic claudication are persistent or recurrent, or when there is onset of a progressive neurologic deficit[11].

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Moreover, slippage of >50% is also an indication for spinal arthrodesis[12-14].

The aim of surgery is to decompress the involved neural structures and fuse the vertebrae. Surgery can be performed with or without reduction of the slipped vertebra.

The aim of reduction is to restore the spinal anatomy and disc space, leading to a substantial realignment of the spinopelvic sagittal plane as measured by the slip angle. Reduction of the vertebra should be considered when there is segmental instability or sagittal imbalance[15-19]. The improvement in biomechanical orientation facilitates arthrodesis and neurologic decompression[20,21]. The role of reduction in the operative management of spondylolisthesis is still controversial because of its potential complications, including neurologic deficits, prolonged operative time, and loss of reduction.

The aim of this systematic review was to compare the clinical and radiographic outcomes of the two different arthrodesis strategies (arthrodesis in situ and arthrodesis following reduction) for the surgical management of high-grade spondylolisthesis.

Materials and Methods

Literature Search and Data Extraction

We undertook a systematic review of the literature according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines by using the PRISMA checklist and algorithm[22,23]. We identified studies addressing the management of high-grade spondylolisthesis by performing a comprehensive search of the PubMed, Ovid MEDLINE, Cochrane, CINAHL, Google Scholar, and Embase databases with use of the keyword "spondylolisthesis" in combination with "surgery," "reduction," "in situ," "low back pain," "high-grade," "lumbar spine," "lumbar instability," and "fusion." All articles relevant to the subject were retrieved, and reviewers hand-searched the bibliographies of all retrieved studies and other relevant publications, including reviews and meta-analyses, for additional relevant articles. A potentially eligible study had to involve patients with spondylolisthesis managed with arthrodesis with or without reduction. Each article was examined to extract data involving patient characteristics, follow-up duration, radiographic measurements, surgical procedures, postoperative pain, and adverse events. Only articles published in peer-reviewed journals were included. Case reports, letter to the editors, and articles not specifically reporting outcomes were excluded. Disagreements were resolved by discussion.

Quality Assessment

The quality of the studies with respect to methodology was assessed with the Coleman Methodology Score. The total score can range from 0 to 100 points, with a higher score indicating that the study better avoids the effects of chance, various biases, and confounding factors. The final score can be categorized as excellent (85 to 100 points), good (70 to 84 points), fair (50 to 69 points), or poor (<50 points). The subsections that make up the Coleman Methodology Score are based on the subsections of the CONSORT (Consolidated Standards of Reporting Trials) statement (for randomized controlled trials)[24].

We modified the Coleman criteria to make them reproducible and relevant for the systematic review of reduction or arthrodesis in situ for the management of spondylolisthesis. Each adopted study was scored independently and in triplicate by three reviewers (U.G.L., M.L., and G.R.). This procedure was performed twice by each author. The studies were also assessed in triplicate with use of the level of evidence rating introduced in the American Volume of *The Journal of Bone and Joint Surgery* in 2003[25] and later updated.

Statistical Analysis

Data for categorical variables are reported as the frequency and the percentage. Data for continuous variables are reported as the mean and the standard deviation or the range with the minimum and maximum values. The Student t test was used to compare the outcomes of the reduction and arthrodesis in situ groups in the included studies. The Pearson chi-square exact test was used to compare the safety of the two procedures. The Student t test was used to compare the mean Coleman Methodology Score values assigned by the three examiners. A p value of <0.05 was considered significant.

When appropriate, the safety of the reduction and arthrodesis in situ procedures was also compared with use of a standard meta-analysis involving a fixed-effects model (Review Manager [RevMan] version 5.1.4; The Nordic Cochrane Center, The Cochrane Collaboration, Copenhagen). Studies providing frequencies of adverse events related to surgery were included into meta-analysis. We examined heterogeneity with use of both a chi-square test and the I^2 statistic, which is the percentage of variability among studies that is due to true differences among studies (heterogeneity) rather than sampling error (chance)[26]. We considered an I^2 value of >50% to reflect substantial heterogeneity[27].

Source of Funding

No funding was received for this study.

Results

An initial database search retrieved 2150 studies. We then performed the search again, restricting it only to comparative studies. Eight studies[18,19,21,28-32], published from 1992 to 2011, that compared arthrodesis in situ with arthrodesis after reduction of the spondylolisthesis were included in the present analysis. All but one[30] of the included studies were retrospective. No randomized clinical trials of spondylolisthesis reduction compared with arthrodesis in situ were identified. Suk et al.[33] performed a comparative study of two different reduction approaches (complete and partial reduction), and that study was therefore excluded from our analysis.

Quality Assessment

The mean value (and standard deviation) of the Coleman Methodology Score was 58 ± 4 points, showing that the mean quality of the included studies was fair. No significant difference was found among the mean Coleman Methodology Score values calculated by the three examiners.

Demographics

Eight studies that included reports of a total of 165 procedures involving reduction followed by arthrodesis and 101 procedures involving arthrodesis in situ without reduction were included in the review. All studies investigated the management of high-grade spondylolisthesis. Five studies involved pediatric patients younger than eighteen years of age (mean age, 14.2 ± 0.6 years)[18,21,28,31,32]. The remaining three studies[19,29,30] involved adult patients (mean age, 40.6 ± 6.2 years). In all eight studies, the main symptom was low back pain. The mean duration of follow-up was 8.0 ± 4.3 years in the pediatric populations and 3.4 ± 2.1 years in the adult populations (see Appendix).

Surgery

In the reduction group, arthrodesis was performed at L5-S1 in ninety-three patients, at L4-S1 in fifty-nine, at L3-S1 in three, at L3-L5 in nine, and at T12-L5 in one. In the arthrodesis in situ group, arthrodesis was performed at L5-S1 in sixty-eight patients, at L4-S1 in twenty-seven, at L3-S1 in five, and at L3-L5 in one. Several arthrodesis techniques were used. In the reduction group,

Study or Subgroup	Reduction Events	Reduction Total	Arthrodesis in situ Events	Arthrodesis in situ Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Burkus et al 1992	2	24	3	18	16.5%	0.50 [0.09, 2.69]
Molinari et al 1999	2	25	5	12	32.5%	0.19 [0.04, 0.85]
Muschik et al 1997	2	30	7	29	34.2%	0.28 [0.06, 1.22]
Poussa et al 1993	1	11	3	11	14.4%	0.33 [0.04, 2.73]
Poussa et al 2006	2	11	0	11	2.4%	5.00 [0.27, 93.55]
Total (95% CI)		**101**		**81**	**100.0%**	**0.41 [0.20, 0.84]**
Total events	9		18			

Heterogeneity: Chi² = 4.15, df = 4 (P = 0.39); I² = 4%
Test for overall effect: Z = 2.45 (P = 0.01)

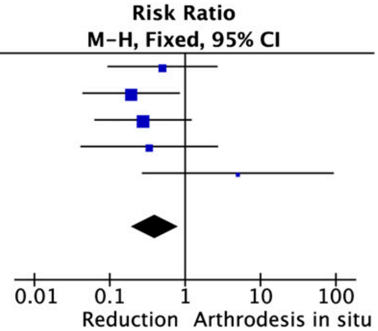

Fig. 1
Forest plot of the risk ratio for developing pseudarthrosis in patients undergoing a reduction procedure compared with patients undergoing arthrodesis in situ. M-H = Mantel-Haenszel, CI = confidence interval, and df = degrees of freedom.

the spinal arthrodesis was circumferential in eighty-seven (53%) of the 165 patients, transforaminal interbody in forty-eight (29%), and posterolateral in thirty (18%). In the arthrodesis in situ group, the spinal arthrodesis was circumferential in twenty-six (26%) of the 101 patients, posterolateral in thirty (30%), anterior interbody in twenty-nine (29%), trans-sacral in thirteen (13%), and transforaminal interbody in three (3%). All spinal arthrodeses in the reduction group were instrumented, whereas only twenty-one (21%) of the procedures in the arthrodesis in situ group were instrumented.

Only three studies[19,21,30], which included sixty-eight patients who underwent reduction and arthrodesis, included descriptions of the amount of reduction achieved by each patient. The reduction was partial in forty-seven (69%) of these sixty-eight patients and complete in twenty-one (31%).

Radiographic Outcomes

The radiographic parameters reported in the studies were the percentage of slippage, slip angle, lumbar lordosis, sacral inclination, and lumbosacral angle (see Appendix)[18,21,28-32]. Only one of the eight studies did not include reporting of any postoperative radiographic measurements[19]. Five studies[18,28,29,31,32] included reporting of the change in the percentage of slippage from the preoperative and immediate postoperative time points to the last follow-up time point. The mean decrease in the percentage of slippage between the preoperative and last follow-up time points was 27.8% ± 13.2% in the reduction group and 3.7% ± 5.9% in the arthrodesis in situ group ($p < 0.002$). Four studies[18,21,28,32] included reporting of the change in the slip angle between the preoperative and last follow-up time points; the mean decrease was 20.9° ± 1.7° in the reduction group and 3.4° ± 3° in the arthrodesis in situ group ($p < 0.003$). Four studies[18,28-30] included reporting of the change in lumbar lordosis between the preoperative and last follow-up time points; the mean increase was 0.5° ± 6.6° in the reduction group and 11.5° ± 7.1° in the arthrodesis in situ group ($p = 0.07$).

Complications

The reported risk of major complications for each of these procedures varied among the included studies, as indicated in the Appendix.

Pseudarthrosis

A pseudarthrosis occurred in nine (5.5%) of the 165 patients in the reduction group and in eighteen (17.8%) of the 101 patients in the arthrodesis in situ group ($p = 0.004$)[18,21,28,31,32]. The analysis of the pooled data showed that the standardized mean risk ratio for developing a pseudarthrosis was 0.4 (95% confidence interval, 0.19 to 0.81) in patients undergoing reduction and arthrodesis compared with patients undergoing arthrodesis in situ ($I^2 = 4\%$, $p = 0.39$ for heterogeneity) (Fig. 1).

Study or Subgroup	Reduction Events	Reduction Total	Arthrodesis in situ Events	Arthrodesis in situ Total	Weight	Risk Ratio M-H, Fixed, 95% CI
De Wald et al 2005	7	16	2	4	25.3%	0.88 [0.28, 2.70]
Gong et al 2010	0	21	3	13	33.8%	0.09 [0.01, 1.63]
Molinari et al 1999	4	25	0	12	5.3%	4.50 [0.26, 77.40]
Muschik et al 1997	1	30	1	29	8.0%	0.97 [0.06, 14.74]
Poussa et al 1993	0	11	1	11	11.8%	0.33 [0.02, 7.39]
Poussa et al 2006	1	11	2	11	15.8%	0.50 [0.05, 4.75]
Total (95% CI)		**114**		**80**	**100.0%**	**0.68 [0.32, 1.49]**
Total events	13		9			

Heterogeneity: Chi² = 4.09, df = 5 (P = 0.54); I² = 0%
Test for overall effect: Z = 0.96 (P = 0.34)

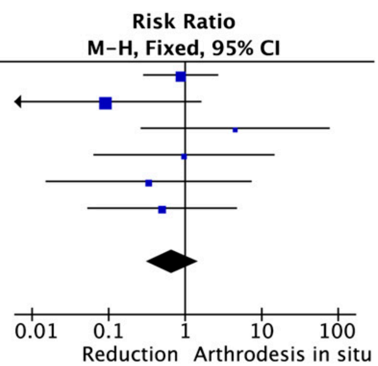

Fig. 2
Forest plot of the risk ratio for developing any neurologic impairment in patients undergoing a reduction procedure compared with patients undergoing arthrodesis in situ. M-H = Mantel-Haenszel, CI = confidence interval, and df = degrees of freedom.

Neurologic Deficits

Neurologic deficits were found in thirteen (7.9%) of the 165 patients in the reduction group and in nine (8.9%) of the 101 patients in the arthrodesis in situ group (p = 0.8)[18,19,21,28,29,32]. The analysis of the pooled data showed that the standardized mean risk ratio for developing any neurologic impairment was 0.72 (95% confidence interval, 0.33 to 1.57) in patients undergoing reduction and arthrodesis compared with patients undergoing arthrodesis in situ (I^2 = 0%, p = 0.54 for heterogeneity). However, the slight elevation in risk associated with arthrodesis in situ was not significant (Fig. 2).

Paresthesia or dysesthesia was found in seven (4.2%) of the 165 patients in the reduction group and five (5.0%) of the 101 patients in the arthrodesis in situ group (p = 1.0)[19,29]. L5 nerve root injury was found in one (0.6%) of the patients in the reduction group and one (1%) of the patients in the arthrodesis in situ group (p = 1.0)[28]. Extensor hallucis longus weakness was found in three (1.8%) of the patients in the reduction group[19,21] and one (1.0%) of the patients in the arthrodesis in situ group (p = 0.56)[29]. Foot drop was found in three (1.8%) of the patients in the reduction group[19,21,32], including one of the patients with extensor hallucis longus weakness[21]. Cauda equina syndrome was found in one (0.6%) of the patients in the reduction group[19]. Peroneal palsy was found in two (2.0%) of the patients in the arthrodesis in situ group[28].

Instrumentation Failure

Instrumentation failure leading to revision surgery was reported in eight (4.8%) of the 165 patients in the reduction group[18,19,21,29]. Causes of failure were pullout or breakage of instrumentation associated with partial loss of reduction. Only one patient had instrumentation failure associated with nonunion; in the remaining patients, the cause of the instrumentation failure was related to the type of instrumentation used. No instrumentation failure event was reported in the arthrodesis in situ group.

Additional Complications

Five (3.0%) of the 165 patients in the reduction group and three (3.0%) of the 101 patients in the arthrodesis in situ group developed a deep wound infection (p = 0.7)[21,29,30-32]; all of the patients were treated nonoperatively. One (0.6%) of the patients in the reduction group and two (2.0%) of the patients in the arthrodesis in situ group had a dural tear (p = 1.0)[21,29]. Three (1.8%) of the patients in the reduction group and six (5.9%) of the patients in the arthrodesis in situ group developed regional lumbar pain (p = 0.14)[32].

Two (1.2%) of the 165 patients in the reduction group developed urinary retention ten days after surgery[21]. Two (2.0%) of the 101 patients in the arthrodesis in situ group and no patients in the reduction group experienced mild superior mesenteric artery syndromes after surgery because of tight postoperative casting[21]. The patients in the reduction group experienced one case (0.6%) each of pulmonary embolus, pancreatitis, iliac vein thrombosis, and transient retrograde ejaculation[19]. The patients in the arthrodesis in situ group experienced one case (1%) each of thrombosis with post-thrombotic syndrome and an intraoperatively damaged iliac vein[32].

Discussion

There is no consensus regarding the best surgical management of high-grade slippage in patients with spondylolisthesis. Few published studies have compared the outcomes of arthrodesis with or without reduction in patients with severe spondylolisthesis[18,19,21,28-32].

The literature supports surgical treatment in patients with spondylolisthesis who have undergone unsuccessful nonoperative management or have evidence of neurologic deficits[14,19,20,28]. In situ posterolateral spinal arthrodesis is widely accepted for the treatment of mild spondylolisthesis; it is also generally considered safe, with good long-term results[5,18,34-37]. However, in addition to not restoring physiologic alignment and balance, such a procedure can be associated with progression of the deformity, especially of the slip angle. Patients with high-grade defects tend to have hyperlordosis of the lumbar spine to compensate for the lumbosacral kyphosis. Posterolateral arthrodesis associated with reduction of the slipped vertebra can provide better alignment of the spinopelvic sagittal plane; however, the prevalences of neurologic deficits and loss of reduction postoperatively have been reported to be greater than with arthrodesis in situ[38]. Correction of the sagittal position of the lumbosacral junction may improve the fusion rate by reducing the shear forces[39-42]. Potential disadvantages of reduction include increased operative time and the possibility of distracting neurologic elements during the corrective procedure.

Our analysis of the pooled data showed that pseudarthrosis was significantly more frequent in the arthrodesis in situ group compared with the reduction group (17.8% compared with 5.5%, p = 0.004). These findings are consistent with previous case series in which nonunion rates of up to 19% and 8% were reported following arthrodesis in situ and arthrodesis following reduction, respectively[43].

Some factors, such as the type and length of the spinal arthrodesis, could have affected the union rates in the two groups. In the present study, the number of patients who underwent circumferential arthrodesis was 53% in the reduction group and 26% in the arthrodesis in situ group, suggesting that circumferential arthrodesis can provide a solid fusion. Single-level arthrodesis at L5-S1 was the most frequently performed procedure in both groups (56% in the reduction group and 67% in the arthrodesis in situ group); however, the percentage of patients who underwent arthrodesis of two or more levels was greater in the reduction group than in the arthrodesis in situ group (44% compared with 33%). All arthrodeses in the reduction group were instrumented, whereas only 21% were instrumented in the arthrodesis in situ group. Finally, the resection of the upper sacrum may prevent nonunion by increasing the area of cancellous bone contact[29].

In our analysis, the neurologic deficits that occurred with reduction were largely transient, and their rate was not significantly greater compared with the rate in the arthrodesis in situ group (7.8% compared with 8.9%, p = 0.8). The overall prevalence of neurologic deficits reported in published case series and retrospective noncomparative studies is greater than that in the included retrospective comparative studies. Indeed, the neurologic risk associated with reduction has been estimated to be between 10% and 50% and usually involved the L5 nerve root and consisted of temporary or partial palsies[16,44-46]; cases of cauda equina syndrome have also been reported[45].

Some factors, such as patient age and the type of spondylolisthesis, appear to affect the prevalence of nerve injuries. The reduction is more difficult and the risk of neurologic impairment is greater in adults compared with pediatric patients[1-3]. The prevalence of neurologic complications is also greater in patients with isthmic spondylolisthesis than in those with degenerative spondylolisthesis[47].

Although several authors have suggested the use of intraoperative neurophysiologic monitoring for high-grade spondylolistheses[19,48,49], only one[21] of the eight included studies used somatosensory evoked potential (SSEP) monitoring as well as an intraoperative wake-up test for neurologic assessment of patients undergoing a reduction procedure.

Evidence-based guidelines for the use of intraoperative neurophysiologic monitoring are lacking[50]. Monitoring of SSEPs has a reported sensitivity of 0% to 52% and specificity of 95% to 100% for the detection of iatrogenic motor deficits[50]. Transcranial motor evoked potentials (MEPs) are standard for the assessment of motor deficits and permit the evaluation of the motor cortex, corticospinal tract, nerve roots, and peripheral nerves. Monitoring of transcranial MEPs has a reported sensitivity of 75% to 100% and specificity of 84% to 100% for the detection of iatrogenic motor deficits[50]. Other methods include spontaneous or triggered electromyography, which have a very high sensitivity for the detection of nerve root injuries during procedures involving instrumentation and arthrodesis[51].

The decision to correct high-grade slippage defects by reduction is still a controversial one. In an attempt to determine which patients should be treated with reduction, some authors have investigated the relationship between sagittal spinal parameters and pelvic morphology and orientation. Patients with high-grade spondylolisthesis could be classified on the basis of the orientation of the pelvis as having a "balanced" or "unbalanced" pelvis. The balanced-pelvis type of spondylolisthesis includes patients with low pelvic tilt and high sacral slope, whereas the unbalanced type includes patients with a retroverted pelvis having high pelvic tilt and low sacral slope[52]. On the basis of this classification, some authors suggest reduction of the deformity, restoring the spinopelvic balance, only in patients with an unbalanced pelvis, whereas arthrodesis in situ without correction would be preferred in patients with a balanced pelvis[52-54].

Although reduction can potentially result in complications, complication rates in the present analysis did not differ between the reduction and arthrodesis in situ groups. On the other hand, reduction of a high-grade spondylolisthesis would improve overall spine biomechanics by correcting the local kyphotic deformity and reducing the vertebral slippage. We manage patients with high-grade spondylolisthesis by performing reduction under intraoperative neurophysiologic monitoring, such as SSEPs combined with spontaneous electromyography. We usually perform a posterolateral or circumferential instrumented arthrodesis.

The major weakness of the present study is the small number of articles that met the inclusion criteria, particularly with regard to high-grade spondylolisthesis in adult patients. Another weakness is the heterogeneity of the surgical treatments performed in each group, both with respect to the type of arthrodesis (e.g., anterior, posterolateral, or circumferential) and the use of instrumentation. These factors prevented us from developing standardized guidelines for the management of these patients.

In conclusion, we found no definite benefit of reduction over arthrodesis in situ except for a significantly lower rate of pseudarthrosis. Further adequately powered randomized trials with appropriate subjective and objective outcome measures are required to establish evidence-based surgical management of high-grade spondylolisthesis.

Appendix

eA Tables summarizing the characteristics of the included studies, and the mean radiographic measurements and complications of surgical management in the included studies are available with the online version of this article as a data supplement at jbjs.org. ■

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