Achieving Optimal Outcome for Degenerative Lumbar Spondylolisthesis: Randomized Controlled Trial Results

Surgery may be offered to patients with symptomatic lumbar stenosis with degenerative lumbar spondylolisthesis who fail nonoperative treatment measures including physical therapy and epidural steroid injections. For patients with lumbar stenosis without spondylolisthesis, a decompression alone is typical and is based on previously published guidelines. Those patients who do have degenerative spondylolisthesis and who also have significant mechanical back pain may be offered lumbar decompression with or without fusion. Recently, conflicting studies have been published in the *New England Journal of Medicine* on the efficacy of decompression alone vs decompression with fusion for the treatment of symptomatic lumbar stenosis with spondylolisthesis.

Patient-reported outcomes have been used over the past decade to demonstrate the efficacy of spinal decompression with or without fusion surgery. There will be an additional emphasis on durability, cost-effectiveness, and ultimately on the value of spinal surgery in the coming decade. This transition to an analysis of cost-effectiveness or value from a previous focus on the efficacy of surgical treatment alone has become an increasingly important priority.

Our goal is to examine the recently published randomized controlled trials that attempt to understand the role of fusion when performing a decompression for the treatment of symptomatic stenosis with spondylolisthesis and to assess the value of the addition of fusion to a decompression in the treatment paradigm.

**ABBREVIATIONS:** MCID, minimum clinically important difference; ODI, Oswestry Disability Index; PCS, physical component summary; SF-36, Short Form - 36; SLIP, Spinal Laminectomy versus Instrumented Pedicle screw fusion trial; SPORT, Spine Patient Outcomes Research Trial

**RANDOMIZED CONTROLLED TRIALS**

In April 2016, the *New England Journal of Medicine* published 2 new randomized clinical trials that examined the utility of adding a fusion when performing a decompressive laminectomy for lumbar stenosis with grade I lumbar spondylolisthesis. The studies reached different conclusions. The Swedish Trial randomized 247 patients with lumbar stenosis with or without spondylolisthesis, and 1 or 2 levels of disease. By not including dynamic lumbar radiographs, this trial did not attempt to differentiate between those patients with radiographic instability (>3 mm motion on dynamic lumbar imaging) or not. This study, which included a heterogeneous population, did not detect any difference in the treatment arms using the Oswestry Disability Index (ODI) as the primary outcome measure.

It should be noted that the Swedish study population might differ from the American population in terms of rate of mechanical low back pain, body mass index, and worker’s compensation litigation status.

The Spinal Laminectomy versus Instrumented Pedicle screw fusion trial (SLIP) study, on the other hand, was a smaller study that focused upon a homogeneous population of patients with nonmobile single-level grade I spondylolisthesis. Patients who underwent fusion in addition to decompression in the SLIP study had superior health-related quality of life, measured using the Short Form-36 (SF-36) physical component summary (PCS) score. This benefit was maintained long term, at 2, 3, and 4 yr following randomization. Since the Swedish study did not analyze single-level spondylolisthesis cases separately, it is not possible to compare the trials directly.

There was no difference detected in the disease-specific ODI instrument, which was the primary outcome measure in the Swedish trial and a secondary outcome in the SLIP study.
However, ODI scores may become better over time, as the data from the SLIP study suggest. The difference in ODI score between groups was 9 points favoring fusion (P = .05) at 4 yr. Using minimum clinically important difference (MCID) = 10 points for ODI, 61% of patients treated with laminectomy alone compared to 85% of patients treated with fusion and laminectomy achieved the MCID (P = .04). The sample size estimate for the SLIP study was based on a previously published pilot study that examined the comparative effectiveness of the addition of lumbar fusion in patients with grade I spondylolisthesis.5 Despite this, it is not clear that either trial was appropriately powered to detect a difference of 10 points even if it existed. The sample size estimate (90% power) for a future trial, assuming a standard deviation of 18, is a total of at least 140 patients with single-level grade I spondylolisthesis to detect a difference of 10 in ODI scores between groups. Future trials would likely inflate these numbers by 10% to 15% to account for interim analyses and expected rates of lost follow-up. There were only 90 patients with single-level lumbar spondylolisthesis in the Swedish study.7 This lack of power is a major concern for focusing upon ODI when analyzing the results of both trials.8

The SLIP study identified a clinically meaningful improvement in health-related quality of life among patients treated with lumbar fusion. The emphasis on health-related quality of life is consistent with a shift to patient centered care, as seen in the orthopedic joint replacement literature and is necessary for the comparison of the impact of different health interventions in our society.9 The level of improvement in health-related quality of life associated with lumbar fusion in the SLIP study is comparable to that of patients who undergo hip arthroplasty.10

**EVIDENCE-BASED PRACTICE GUIDELINES**

The latest version of the “Guidelines for the performance of lumbar fusion” indicated a grade B level recommendation providing moderate support for the performance of fusion in conjunction with decompression in patients with neurogenic claudication or radiculopathy due to stenosis associated with spondylolisthesis.11 While the Spine Patient Outcomes Research Trial (SPORT) study did not specifically address the issue of decompression alone vs decompression plus fusion, it provided the highest quality of evidence available at that time. The study provided level II evidence from a high-quality cohort study indicating that patients treated with laminectomy and fusion did significantly better than patients treated nonoperatively. We have recently published a more detailed analysis of how these randomized controlled trials contribute to the current evidence base.8

The Swedish study patient population was heterogeneous in terms of radiographic diagnoses and number of levels treated. The paper provides level II evidence that the addition of a variety of fusion techniques does not have significant benefit in the first 2 yr following operation compared to a variety of decompression techniques in a heterogeneous population of patients with stenosis associated with spondylolisthesis.3

The SLIP study provides level I evidence for the efficacy of fusion to improve clinical outcomes and lower re-operation rates compared to a standard laminectomy and medial facetectomy over a 4-yr time frame in patients with neurogenic claudication associated with stable single level spondylolisthesis. The study does not provide evidence regarding the utility of fusion in patients with multilevel disease and does not offer evidence regarding the utility of newer minimally invasive decompression and fusion techniques.8

It is important to recognize that the patient populations treated, surgical techniques used, and outcomes measures assessed differed between the 2 studies, making it no surprise that results would appear to conflict on superficial review. The principle of applying a standard surgical approach to all comers with spondylolisthesis is not supported by either study. Furthermore, benefits of fusion are not anticipated to be realized in 1 or 2 yr and the authors of both studies are strongly encouraged to follow their respective patient cohorts as long as possible to be able to detect differences in late reoperation rates or deterioration in function due to instability or adjacent segment degeneration. Given the present state of the literature, either fusion or nonfusion techniques may be appropriate depending on the patients’ anatomy, lifestyle, and desires. This issue will require ongoing study, especially with the advent of minimally invasive techniques for both decompression and fusion.8

**THE VALUE OF LUMBAR FUSION FOR DEGENERATIVE SPONDYLOLISTHESIS**

One of the strengths of the Swedish study is that direct costs from a single payer system and indirect costs were specifically collected over the first 2 yr of the study.3 The SLIP study is also ideally suited for a cost-effectiveness study, but a formal economic analysis has not been completed at the present time. In order to measure the comparative cost-effectiveness of these 2 interventions for patients with lumbar spondylolisthesis, a broad economic analysis that includes both direct and indirect costs (including loss of productivity) will need to be performed over a long period of time—at least over 5 yr.

Durability, defined as maintenance of clinical benefit without the need for additional interventions, is dependent on complete and reliable long-term follow-up that is often difficult to obtain even in high-quality studies. Prior studies have shown that costly interventions such as lumbar fusion may ultimately be cost-effective if they provide durable clinical benefit.12,18 The issue of durability represents the most substantial discrepancy between the Forsth3 and Ghogawala4 studies, and is likely to determine the actual cost-effectiveness of fusion for lumbar spondylolisthesis and spinal stenosis. In addition, hospital length of stay was significantly greater in the Swedish study making economic analyses from the Swedish study not likely to be relevant for
American stakeholders. Ghogawala reports a substantially higher revision rate in patients treated without fusion, whereas Forsth reports equivalent revision rates.3,4 Forsth et al3 suggest that the higher revision rate observed in the Ghogawala study4 reflects the surgeon’s belief that a subsequent fusion procedure might address residual symptoms after decompression alone. While this explanation might be accurate in some cases, multiple alternative explanations include cultural bias toward revision surgery or a more supportive social safety net for patients unable to resume normal function in Sweden. The SLIP investigators did demonstrate a significant improvement in both ODI and SF-36 PCS scores after fusion was performed in patients who developed instability following lumbar laminectomy (Figure 1).6 Regardless of the rationale, decompression and fusion may ultimately be more cost-effective than decompression alone if revision surgery is less common following lumbar fusion in the USA, despite its higher initial cost.

**SLIP II—OPPORTUNITIES AND FUTURE DIRECTIONS**

Randomized clinical trials often produce high-quality data relative to the study question, but new questions may arise when similar trials generate conflicting results. The differences in the SLIP study and Swedish study populations make direct comparison of the results difficult, despite the fact that both trials examine the role of lumbar fusion in patients with spinal stenosis and spondylolisthesis.8 The studies, taken together, do underline the need for a better definition of clinically relevant instability in these patients. Patient populations should be defined as specifically as possible in future studies that aim to compare the effectiveness of different surgical strategies and perhaps include more extensive stored radiographic data for future analysis.

The SLIP study investigators have just organized and obtained funding for a nonrandomized registry study called SLIP II. SLIP II will enroll 1000 patients with grade I degenerative lumbar spondylolisthesis from at least 10 North American sites and will follow these patients for 5 yr. Primary outcome measures will be the ODI and EQ-5D. A formal cost-effectiveness analysis is planned. SLIP II will include an international expert panel review by experienced orthopedic and neurological spine surgeons (Table).14,15 Each patient’s lumbar MRI (sagittal and key axial images and flexion and extension radiographs) will be uploaded into a web-based platform and reviewed with plans to share the reviews with patients in real time (Figure 2). Figure 2 shows

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*Ten to 12 sites will be engaged as enrolling sites.*
the importance of defining the patient population using radiographic data. The first patient has single-level spondylolisthesis with stenosis and was included in the SLIP study. The second patient’s imaging demonstrates 2 levels of pathology and would therefore have been eligible for the Swedish study but would not have been eligible for the SLIP study. The objective of the panel review will be to provide patients access to expert opinion based on current evidence.
SUMMARY OF THE KEY POINTS

• The SLIP study provides level I evidence supporting that decompression with fusion is superior to decompression alone using a valid health-related quality of life outcome at 2, 3, and 4 yr.

• One-third of patients in the SLIP study developed instability within 4 yr after lumbar laminectomy was performed for lumbar stenosis with degenerative lumbar spondylolisthesis.

• Patients treated with either decompression alone or decompression with lumbar fusion improve in terms of quality of life.

• Seventy per cent of patients treated with decompression alone appear to do very well.

The key question raised by the SLIP study is how to determine a priori whether a patient will be stable following lumbar laminectomy in the context of grade I spondylolisthesis. One of the major goals of SLIP II will be to produce enough clinical data for analysis in order to guide individual patients and their treating surgeons about the optimal utilization of fusion or not when treating patients with grade I degenerative spondylolisthesis and lumbar stenosis.

Disclosures

Dr Ghogawala was the lead author of the SLIP study, which was published in the New England Journal of Medicine. Dr Dziura was the lead biostatistician for the SLIP study. Dr Mummaneni is a consultant for DePuy Spine and Stryker Spine, has received honoraria from AO Spine and Globus, royalties from DePuy Spine, Thieme Publishing, and Springer Publishing, and is a stock holder in Spincity/ISD. Dr Glassman receives royalties from and consults for Medtronic, Nuvasive, and Zimmer-Biomet, consults for K2M and Stryker, and is a stock holder in Nuvasive. The other authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

REFERENCES


