

Weinstein JN, Lurie JD, et al. Surgical versus Nonsurgical Treatment for Lumbar Degenerative Spondylolisthesis. N Engl J Med 2007;356:2557-70.

Design: Randomized clinical trial

Population/sample size/setting:

- 601 patients (412 women, 189 men, mean age 66) with lumbar degenerative spondylolisthesis and spinal stenosis treated at 13 centers in 11 US states, divided into two cohorts, one randomized and one observational
 - o 304 patients were in the randomized cohort and 303 were in the observational cohort; 6 patients did not contribute data, leaving cohorts of 301 and 300 respectively in the randomized and observational cohorts
 - o Only patients who consented to randomization were enrolled in that cohort; any patient who had a surgical/nonsurgical treatment preference was enrolled in the observational cohort
- Eligibility criteria were neurogenic claudication or radicular leg pain with associated neurological signs, spinal stenosis on cross-sectional imaging, and degenerative spondylolisthesis on lateral x-ray when the patient is standing
- All patients had been persistently symptomatic for at least 12 weeks and had been confirmed as surgical candidates by their physicians
- Isthmic spondylolisthesis and spondylolysis were exclusion criteria, but adjacent level stenosis was not an exclusion criterion
- Patients in the randomized cohort received treatment assignments from a computer-generated allocation list; patients in the observational cohort chose their treatment with their physician

Main outcome measures:

- The 304 patients in the randomized cohort were allocated to surgery (n=159) or nonsurgical treatment (n=145)
- The 303 in the observational cohort chose surgery (n=173) or nonsurgical treatment (n=130)
- 86% of patients had a Grade 1 slip and 14% had a grade 2 slip
- Stenosis was graded as severe in 60% of patients; 35% had multiple levels of stenosis
- Surgery consisted of standard posterior decompressive laminectomy with or without bilateral single-level fusion
 - o The vast majority (94%) of the operative procedures included fusion; 73% with instrumentation and 21% without instrumentation; only 6% of operated patients had decompression only
 - o 27% of the operated patients had multilevel fusion
 - o 66% of operated patients had decompression at more than one level; 33% had one level decompression
- Nonsurgical protocol included at least a form of active physical therapy, education/counseling for home exercise, and NSAIDs; 45% had epidural steroids and 34% had opiates during the study

- Primary outcomes were two scales of the SF-36 (body pain and physical function) and the Oswestry Disability Index (ODI), and were measured at 6 weeks, and at 3, 6, 12, and 24 months
 - o Primary analysis compared groups on changes from baseline at each follow-up time
- Secondary outcomes included patient-reported improvement and satisfaction
- The initial analysis of the randomized cohort was by intention to treat, but there was extensive crossover, and later analyses were based on treatment actually received
 - o 57% of those randomized to surgery had it within 12 months, and 64% had it by 2 years; the remaining 36% had not had surgery at the 2 year mark
 - o 44% of those randomized to nonsurgical care had surgery in the first 12 months, and 49% had had surgery by 2 years
- In the intention-to-treat analysis of the randomized cohort, there were no statistically significant effects for the primary outcomes on the basis of a global hypothesis test for differences in mean changes from baseline
- As-treated analyses were done for the combined observational and randomized cohorts, and showed effects in favor of surgery for all time periods up to 2 years
 - o For SF-36 body pain, the treatment effect at 2 years was 18.1 on a scale of 100; for SF-36 physical function the effect was 18.3 points, and for the ODI the effect was 16.7 points on a scale of 100
 - o The as-treated effects at 2 years were nearly identical in the randomized and observational cohorts
- Subgroup analyses did not show significant treatment effect modification according to age, smoking, treatment preference, duration of symptoms, number of stenotic levels, number of coexisting conditions, severity of stenosis at baseline, or SF-36 mental component score
- Patients undergoing surgery in the combined cohort were younger and more likely to be receiving compensation (workers' comp or social security) than patients receiving nonsurgical care; they also had worse pain, function, and disability than the nonoperative patients
- The reoperation rate at 1 year was 0.6% for recurrent stenosis or spondylolisthesis; and the rate was 3% at 2 years

Authors' conclusions:

- Although intention-to-treat analysis found no significant advantage of surgery over nonsurgical care, that analysis was severely limited by crossover from one group to another
- As-treated analysis showed that surgery was superior to nonoperative treatment as early as 6 weeks, and this advantage persisted at 2 years
- These results are consistent with earlier comparisons of surgical and nonoperative interventions for the same conditions
- There was little harm from either treatment; the patients who did not have surgery moderately improved from baseline to the end of the study

- Although there was great heterogeneity in nonoperative treatment, the interventions received by those patients were in accord with published guidelines
- There were differences in details of surgical procedures between patients, but the study was not able to compare the efficacies of different operations

Comments:

- SPORT studies were set up in a way to permit patients to choose whether to enroll in the randomized trial or in the observational cohort; large crossover was observed in the trials of herniated disc and spinal stenosis without spondylolisthesis as well
- When crossover is large and nonrandom (patients crossing to surgery doing so on the basis of worsening symptoms), the intention-to-treat analysis will underestimate the treatment effect likely to be seen outside the clinical trial
- Because of the very narrow differences between the as-treated analyses in the randomized and observational cohorts, it is reasonable to combine them as the authors did

Assessment: High quality study supporting good evidence that decompression and fusion, with or without instrumentation, of lumbar stenosis with degenerative spondylolisthesis leads to better 2 year outcomes for patients whose symptoms are severe. However, patients who choose nonoperative treatment can also expect their symptoms to improve with nonsurgical treatment, and nonoperative treatment is acceptable if this is the patient preference.