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RANDOMIZED TRIAL

Decompression and Coflex Interlaminar Stabilization Compared With Decompression and Instrumented Spinal Fusion for Spinal Stenosis and Low-Grade Degenerative Spondylolisthesis

Two-Year Results From the Prospective, Randomized, Multicenter, Food and Drug Administration Investigational Device Exemption Trial

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Study Design. Prospective, randomized, multicenter, Food and Drug Administration Investigational Device Exemption trial.

Objective. To evaluate the safety and efficacy of Coflex interlaminar stabilization compared with posterior spinal fusion in the treatment of 1- and 2-level spinal stenosis and degenerative spondylolisthesis.

Summary of Background Data. Long-term untoward sequelae of lumbar fusion for stenosis and degenerative spondylolisthesis have led to the search for motion-preserving, less-invasive alternatives.

Methods. Three hundred twenty-two patients (215 Coflex and 107 fusions) from 21 sites in the United States were enrolled between 2006 and 2010. Subjects were randomized to receive laminectomy and Coflex interlaminar stabilization or laminectomy and posterolateral spinal fusion with spinal instrumentation in a 2:1 ratio. Overall device success required a 15-point reduction in Oswestry Disability Index, no reoperations, no major device-related complications, and no postoperative epidural injections.

Results. Patient follow-up at minimum 2 years was 95.3% and 97.2% in the Coflex and fusion control groups, respectively. Patients taking Coflex experienced significantly shorter operative times ($P < 0.0001$), blood loss ($P < 0.0001$), and length of stay ($P < 0.0001$). There was a trend toward greater improvement in mean Oswestry Disability Index scores in the Coflex cohort ($P = 0.075$). Both groups demonstrated significant improvement from baseline in all visual analogue scale back and leg parameters. Patients taking Coflex experienced greater improvement in Short-Form 12 physical health outcomes ($P = 0.050$) and equivalent mental health outcomes. Coflex subjects experienced significant improvement in all Zurich Claudication Questionnaire outcomes measures compared with fusion (symptom severity [$P = 0.023$]; physical function [$P = 0.008$]; satisfaction [$P = 0.006$]). Based on the Food and Drug Administration composite for overall success, 66.2% of Coflex and 57.7% of fusions succeeded ($P = 0.999$), thus demonstrating noninferiority. The overall adverse event rate was similar between the groups, but Coflex had a higher reoperation rate (10.7% *vs.* 7.5%, $P = 0.426$). At 2 years, fusions exhibited increased angulation ($P = 0.002$) and a trend toward increased translation ($P = 0.083$) at the superior adjacent level, whereas Coflex maintained normal operative and adjacent level motion.

Conclusion. Coflex interlaminar stabilization is a safe and efficacious alternative, with certain advantages compared with lumbar spinal fusion in the treatment of spinal stenosis and low-grade spondylolisthesis.

Key words: Coflex interlaminar stabilization, spinal fusion, spinal stenosis, degenerative spondylolisthesis.

Level of Evidence: 1

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The recent Spine Patient Outcomes Research Trial (SPORT) studies and others have demonstrated clear superiority of laminectomy compared with conservative care at 4 years, and have confirmed the use and cost-effectiveness of this most commonly performed spinal procedure in the spinal stenosis population.[1–4]

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In the setting of spinal stenosis with significant low back pain, however, and in low-grade spondylolisthesis, laminectomy alone has limitations.[1,2,5–12] Kleinstuck *et al*[10] recently reported results from the Spine Society of Europe Spine Tango Spine Surgery Registry and demonstrated that patients with spinal stenosis and predominant low back pain symptoms who underwent laminectomy alone had significantly worse clinical outcomes compared with those patients with a predominance of leg pain. Others have reported similar findings, indicating that baseline low back pain predominance portends a significantly worse clinical outcome when decompression alone is performed.[7,9,11,13,14] Not only may long-term low back pain relief not be achieved, but progression of sagittal plane instability may also be seen in absence of spinal fusion.[6,7,13,15] Consequently, spinal fusion is commonly performed in this setting to treat neurogenic claudication, to achieve motion segment stabilization, and to address the low back pain.[10,12,15]

Although spinal fusion is the current "gold standard" treatment for patients with degenerative spondylolisthesis[6,11,15,16] and is commonly performed in patients with spinal stenosis and significant back pain,[4,10,12] there are well-documented adverse sequelae.[17–20] Alteration of the biomechanical environment may lead to symptomatic adjacent segment disease requiring further surgery and extension of the fusion.[18–28] With pedicle screw instrumentation, there exists risk to the neurovascular structures and instrumentation problems, as well as the potential for development of symptomatic pseudarthrosis, and chronic pain from the iliac crest bone graft harvest site.[17,29] The need for less-invasive, motion-preserving alternatives that include a direct spinal decompression with motion segment stabilization is clear.

In this study, we report the 2-year clinical, radiographical, and safety results from the randomized, multicenter, prospective Food and Drug Administration (FDA) Investigational Device Exemption trial comparing decompression and Coflex (paradigm spine, LLC, New York, NY). Interlaminar stabilization with decompression and posterior spinal fusion with pedicle screw instrumentation for the treatment of spinal stenosis with low back pain, and up to grade 1 degenerative spondylolisthesis (Figure 1). We hypothesize that the Coflex interlaminar non-fusion device will produce a similar or improved safety and efficacy profile when compared with the current "gold standard," lumbar spinal fusion.

MATERIALS AND METHODS

Study Design

The US FDA approved commencement of the Coflex Investigational Device Exemption study on April 12, 2006. The approved study design was a multicenter, prospective randomized trial at 21 US sites. Institutional review board approvals were obtained prior to study initiation at all sites. Randomization according to 2:1 ratio of investigational to control devices was performed within site and number of levels treated based on computer generated randomization codes that was centralized by the study sponsor. Site study personnel were blinded to the treatment assignment up until 5 days prior to surgery and study subjects were blinded until after surgery.

Figure 1. Unimplanted Coflex device.

Patient Population

Patients between the ages of 40 and 80 were required to meet strict inclusion and exclusion criteria for study entry (Tables 1 and 2). There were 2 patient populations that were potential candidates for study enrollment: (1) patients with moderate spinal stenosis with low back pain, and (2) up to Meyerding grade I (*i.e.*, ≤25% sagittal plane translation on flexion-extension radiography) spondylolisthesis (Figure 2 A–C).[30] In order to include only those patients with significant back pain complaints in addition to symptoms arising from spinal stenosis, 2 stringent criteria were required for study entry: (1) minimum Oswestry Disability Index (ODI) of 20 for 50 (40%), and (2) visual analogue scale (VAS) back pain score of 50 for 100 or more.

Clinical Outcomes Measures

Standard clinical outcomes measures were assessed for each patient at baseline, 6 weeks, 3 months, 6 months, 12 months, 18 months, and 24 months postoperatively. Outcomes assessed included ODI, Short-Form 12 (SF-12), Zurich Claudication Questionnaire (ZCQ), and VAS back and leg pain assessments. Neurological success was determined by maintenance or improvement of motor, sensation, and reflex neurological outcomes.

TABLE 1. Inclusion Criteria

Inclusion Criteria
1. Radiographical confirmation of at least moderate lumbar stenosis, which narrows the central spinal canal at 1 or 2 contiguous levels from L1–L5 that require surgical decompression. Moderate stenosis is defined as more than 25% reduction of the anteroposterior dimension compared with the next adjacent normal level, with nerve root crowding compared with the normal level, as determined by the investigator on CT Scan or MRI. The patient may have, but is not required to have for inclusion in the study:
a. Facet hypertrophy and subarticular recess stenosis at the affected level(s);
b. Foraminal stenosis at the affected level(s);
c. Up to grade I stable degenerative spondylolisthesis (Meyerding classification) or equivalent retrolisthesis as determined by flexion/extension radiograph:
i. For single-level disease, there may be up to a grade I stable spondylolisthesis or equivalent retrolisthesis at the affected level as determined on flexion/extension films by the investigator.
ii. For 2-level disease, there may be up to a grade I stable spondylolisthesis or equivalent retrolisthesis at only 1 of the 2 contiguous affected levels, as determined on flexion/extension films by the investigator. Patients with up to grade I stable spondylolisthesis at 2 contiguous levels are excluded, but patients with up to grade I stable spondylolisthesis at 1 level and equivalent retrolisthesis at the adjacent level may be included.
d. Mild lumbar scoliosis (Cobb angle up to 25°).
2. Radiographical confirmation of the absence of angular or translatory instability of the spine at index or adjacent levels (instability as defined by White & Panjabi: Sagittal plane translation >4.5 mm or 15% or sagittal plane rotation >15° at L1–L2, L2–L3, and L3—L4; >20° at L4–L5 based on standing flexion/extension radiographs).
3. VAS back pain score of at least 50 mm on a 100 mm scale.
4. Neurogenic claudication as defined by leg/buttocks or groin pain that can be relieved by flexion such as sitting in a chair.
5. Patient has undergone at least one epidural injection at any prior time point, and at least 6 mo of prior conservative care without adequate and sustained symptom relief.
6. Age between 40 and 80 yr.
7. Oswestry Low Back Pain Disability Questionnaire score of at least 20/50 (40%).
8. Appropriate candidate for treatment using posterior surgical approach.
9. Psychosocially, mentally, and physically able to comply fully with this protocol, including adhering to scheduled visits, treatment plan, completing forms, and other study procedures.
10. Personally signed and dated informed consent document prior to any study-related procedures indicating that the patient has been informed of all pertinent aspects of the trial.

CT indicates computed tomography; MRI, magnetic resonance imaging.

Radiographical Outcomes Measures

In the Coflex cohort, upright neutral lateral, flexion and extension radiographs were obtained at each time point. In the fusion control cohort, the same radiographical data was obtained, with the exception of flexion and extension radiographs, which were withheld at the 6-week and 3-month time points. All radiographical images were sent from the study sites directly to and were evaluated by an independent core radiographical laboratory (Medical Metrics Inc., Houston, TX).

Statistical Analysis Plan

The primary efficacy endpoint for this study is month 24 Composite Clinical Success. To achieve month 24 composite clinical success, a patient's device must "survive" to at least relative day 730 (*i.e.*, no reoperation, revision, removal, or supplemental fixation on or before the exact surgical 2-year anniversary). Additionally, the patients must not have received any epidural injection postoperatively on or prior to their month 24 clinic visit. Other requirements included an ODI improvement from baseline to the month 24 visit of at least 15 points, no persistent new or worsening sensory or motor deficit, and no major device-related complications. Group comparisons included *t* tests for comparing means, computation of standardized effect sizes (mean difference divided by pooled standard deviation), χ^2 and Fisher exact tests to compare categorical outcomes, graphical analyses, and correlational analyses.

RESULTS

Patient Follow-up

Analysis of patient accountability revealed a 24-month clinical and radiographical follow-up rate of 95.3% and 97.2% for the investigational Coflex and fusion control cohorts, respectively. Within-window follow-up rate for the entire randomized cohort was 89% for both Coflex and fusion controls.

TABLE 2. Exclusion Criteria

Exclusion Criteria
• More than 2 vertebral levels requiring surgical decompression.
• Prior surgical procedure that resulted in translatory instability of the lumbar spine [as defined by White & Panjabi].[31]
• More than 1 surgical procedure at any combination of lumbar levels.
• Prior fusion, implantation of a total disc replacement, complete laminectomy, or implantation of an interspinous process device at any lumbar level.
• Radiographically compromised vertebral bodies at any lumbar level(s) caused by current or past trauma or tumor (*e.g.*, compression fracture).
• Severe facet hypertrophy that requires extensive bone removal that would cause instability.
• Isthmic spondylolisthesis or spondylolysis (pars fracture).
• Degenerative lumbar scoliosis (Cobb angle > 25°).
• Disc herniation at any lumbar level requiring surgical intervention.
• *Osteopenia*: A screening questionnaire for osteopenia, SCORE (simple calculated osteoporosis risk estimation), will be used to screen patients who require a DEXA bone mineral density measurement. If DEXA is required, exclusion will be defined as a DEXA bone density measured *T* score of ≤ −1.0 (The World Health Organization definition of osteopenia).
• Back or leg pain of unknown etiology.
• Axial back pain only, with no leg, buttock, or groin pain.
• Morbid obesity defined as a body mass index >40.
• Pregnant or interested in becoming pregnant in the next 3 years.
• Known allergy to titanium, titanium alloys, or MR contrast agents.
• Active or chronic infection—systemic or local.
• Chronically taking medications or any drug known to potentially interfere with bone/soft tissue healing (*e.g.*, steroids), not including a Medrol (Methylprednisolon) dose pack.
• History of significant peripheral neuropathy.
• Significant peripheral vascular disease (*e.g.*, with diminished dorsalis pedis or posterior tibial pulses).
• Unremitting back pain in *any* position.
• Uncontrolled diabetes.
• Known history of Paget disease, osteomalacia, or any other metabolic bone disease (excluding osteopenia, which is addressed earlier).
• Cauda equina syndrome, defined as neural compression causing neurogenic bowel (rectal incontinence) or bladder (bladder retention or incontinence) dysfunction.
• Fixed and complete motor, sensory, or reflex deficit.
• Rheumatoid arthritis or other autoimmune diseases.
• Known or documented history of communicable disease, including AIDS, HIV, active hepatitis.
• Active malignancy: a patient with a history of any invasive malignancy (except nonmelanoma skin cancer), unless he/she has been treated with curative intent and there has been no clinical signs or symptoms of the malignancy for at least 5 years. Patients with a primary bony tumor are excluded as well.
• Prisoner or ward of the state.
• Subject has a history of substance abuse (*e.g.*, recreational drugs, narcotics, or alcohol).
• Subject is currently involved in a study of another investigational product for similar purpose.
• Currently seeking or receiving workman's compensation.
• In active spinal litigation.

Primary location for DEXA scan should be the spine. In the event that the spine T score is in the osteopenic range (−1.0 to −2.5) then a T score from the hip may be obtained. If the T score from the hip comes back above −1.0 then, at the discretion of the investigator, the patient may be considered for inclusion in the study. Also, a hip DEXA may be used in the event that a spine DEXA cannot be obtained.

HIV indicates human immunodeficiency virus; DEXA, dual-energy X-ray absorptiometry.

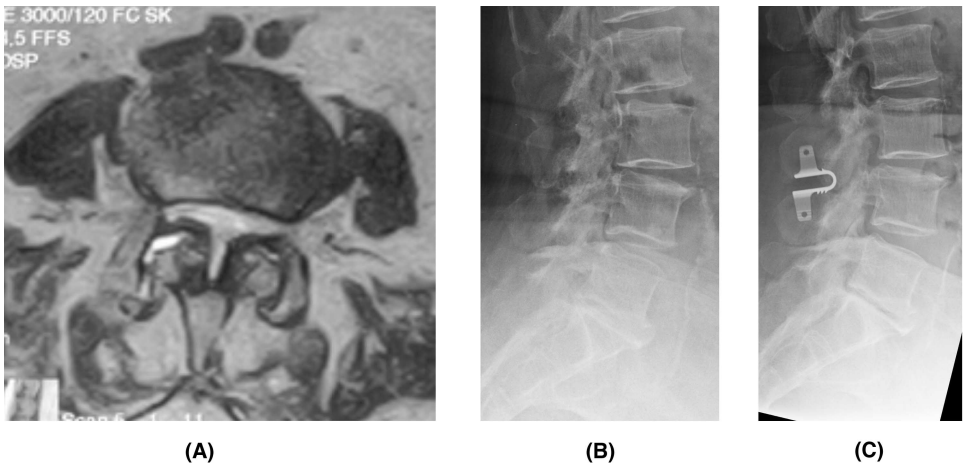

Figure 2. (**A**) Preoperative axial MRI at L3–L4 showing moderate to severe stenosis with facet arthropathy. (**B**) Preoperative lateral radiograph. (**C**) Implanted L3–L4 Coflex interlaminar device.

Demographic Data

At baseline there were no significant differences with respect to age, sex, body mass index, type of stenosis, smoking status, types of conservative care received prior to undergoing surgery, medical comorbidities, and duration of pain prior to undergoing surgery. The average age (standard deviation, range) for the Coflex cohort was 62.1 (9.2, 41–81) years, while the average age for the fusion control cohort was 64.1 (9.0, 41–82) years. Moreover, there were no differences at baseline with respect to ODI, ZCQ, and VAS scores for back and leg pain. The presence or absence of foraminal and subarticular stenosis was measured in addition to the requirement for central stenosis. A total of 6.8% of the patients had central stenosis alone, while 25.5% had central stenosis with foraminal stenosis, 17.4% had central stenosis with subarticular stenosis, and 50.3% had central stenosis with both foraminal and subarticular stenosis. The proportion of patients with spondylolisthesis was similar (Coflex: 99/215 = 46.0%; fusion controls: 51/107 = 47.7%). In the fusion cohort, 52 of 107 (48.6%) of control subjects had iliac crest bone graft harvested for graft material, and 90 of 107 (84.1%) had local bone from the decompression used for graft material. All fusion subjects received pedicle screw instrumentation, but no intervertebral cages or bone morphogenetic proteins were used.

Narcotic Usage

The proportion of fusion control subjects that required narcotic medications was higher at baseline and at all postoperative time points compared with patients taking Coflex; however, this difference was statistically significant only at the 12-month time point ($P = 0.041$). At baseline the rate of narcotic use was 1.2% higher in the fusion cohort ($P = 0.91$), and at 24 months, the rate of narcotic utilization was 10.3% higher in the fusion controls (33.6% fusion, 23.3% Coflex cohort, $P = 0.061$).

Perioperative Outcomes

Table 3 depicts the significantly improved perioperative outcomes with Coflex compared with fusion. Patients taking Coflex had significantly shorter operative times (98.0 *vs.* 153.2 min, $P < 0.0001$), estimated blood loss (109.7 *vs.* 348.6 mL, $P < 0.0001$), and length of stay (LOS) (1.90 *vs.* 3.19 d, $P < 0.0001$) compared with fusion controls. These overall differences were most pronounced in the 2-level patients where the average LOS for patients taking Coflex was 1.97 days compared with 3.74 days for fusion ($P < 0.0001$).

Clinical Outcomes

Oswestry Disability Index

Table 4 depicts the mean ODI scores over time and shows that while the ODI scores were nearly identical at baseline, the Coflex cohort experienced a trend toward better outcomes at 24 months (Coflex: 22.0; fusion: 26.7, $P = 0.075$). Significant improvements were also seen in the Coflex cohort at 6 weeks ($P = 0.001$) and 3-month ($P = 0.033$) postoperative time points. Further, there was a greater proportion of patients taking Coflex achieving a 15-point reduction in ODI at 24 months (Coflex: 85.8%; fusion: 76.7%, $P = 0.08$).

Short-Form 12

There were no baseline differences with respect to either the Physical Component or Mental Component of the SF-12. At 24 months, SF-12 physical component scores had improved significantly more from baseline in the Coflex cohort (15.5 points) compared with fusion controls (12.6, $P = 0.050$). Significant improvements in the Coflex cohort compared with fusion controls were also seen at 6 weeks ($P = 0.048$), 3 months ($P = 0.032$). There were no group differences in SF-12 mental health outcomes measures (Table 5).

Visual Analogue Scale

VAS scores were tabulated for both low back pain, and for the (worse) leg pain. At baseline, VAS back and leg symptoms were similar. There was significant improvement from baseline in all VAS back and leg pain parameters in both groups at each postoperative time point (data not shown). There were no group differences at baseline or at 24 months as depicted in Table 6. In the early postoperative period, however, the

TABLE 3. Summary of Operative Details Continuous Variables Coflex and Fusion Control Randomized Cohorts

	Coflex			Control				Effect
1- and 2-Level Procedures	N	Mean	SD	N	Mean	SD	*P**	Size
Hospital LOS (d)	215	1.90	1.08	107	3.19	1.61	0.000	−1.01
Estimated blood loss (mL)	215	109.7	120.0	105	348.6	281.8	0.000	−1.27
Operative time (min)	214	98.0	41.1	107	153.2	55.5	0.000	−1.19
1-level procedures	N	Mean	SD	N	Mean	SD		
Hospital LOS (d)	138	1.86	1.14	68	2.87	1.45	0.000	−0.81
Estimated blood loss (mL)	138	98.0	96.3	66	290.9	207.7	0.000	−1.36
Operative time (min)	137	90.8	44.0	68	142.0	56.0	0.000	−1.06
2-level procedures	N	Mean	SD	N	Mean	SD		
Hospital LOS (d)	77	1.97	0.95	39	3.74	1.74	0.000	−1.40
Estimated blood loss (mL)	77	130.5	152.1	39	446.2	358.4	0.000	−1.31
Operative time (min)	77	110.9	31.8	39	172.7	49.3	0.000	−1.60

**Two sample pooled t test P value.*
LOS indicates length of stay; SD, standard deviation.

Coflex cohort had a trend toward significantly lower VAS back pain scores at 3 months ($P = 0.062$) and 6 months ($P = 0.063$). VAS leg pain score was significantly better in the Coflex cohort at 3 months ($P = 0.019$) and a trend at 6 months ($P = 0.058$), but not statistically different at any other time point.

Zurich Claudication Questionnaire

At baseline there were no differences in any ZCQ domain. At 24 months, however, patients taking Coflex had significant improvement in each of the ZCQ domains. Specifically, there was statistically significant improvement with Coflex compared with fusion controls at 24 months with respect to ZCQ symptom severity (Coflex: 1.98; fusion: 2.23, $P = 0.023$), ZCQ physical function (Coflex: 1.56; fusion: 1.80, $P = 0.008$), and ZCQ satisfaction (Coflex: 1.42; fusion: 1.65, $P = 0.006$). There were also significant improvements seen compared with fusion controls at earlier time points, including 6 weeks (symptoms severity: $P = 0.008$; physical function: $P = 0.010$; satisfaction: $P < 0.001$), 3 months (physical function: $P = 0.007$; satisfaction: $P = 0.005$), and 6 months (satisfaction: $P = 0.006$), as indicated in Table 7.

Radiographical Outcomes

Quantitative Radiographical Data

Table 8 demonstrates that the index level range of motion was maintained with Coflex, while fusion subjects exhibited an expected significant decrease in the index level range of motion. This difference was statistically significant ($P < 0.0001$) and is consistent with radiographical criteria for fusion. At the superior adjacent level, the Coflex cohort exhibited a similar range of motion to baseline at 24 months. In contrast, the fusion group demonstrated significantly greater superior adjacent level range of motion when compared with Coflex ($P = 0.002$).

TABLE 4. Coflex and Fusion Control Randomized Cohorts Descriptive Statistics for ODI Score

	Coflex Total Score				Fusion Control Total Score				*t* test	Effect
	N	Mean	SD	Median	N	Mean	SD	Median	*P**	Size†
Preoperative	215	60.8	11.8	60.0	107	60.7	11.5	60.0	0.946	0.01
Month 24	162	22.0	18.6	20.0	86	26.7	21.3	23.0	0.075	−0.24

**Two sample pooled t test P value.*
†Standardized effect size (group difference in means divided by pooled within group SD). Smaller values of the ODI reflect less disability. Therefore, negative effect sizes reflect less disability in the group implanted with the investigational device relative to control.
SD indicates standard deviation; ODI, Oswestry Disability Index Score.

TABLE 5. Coflex and Fusion Control Randomized Cohorts Descriptive Statistics for the SF-12 Physical and Mental Health Component Scores

	Coflex Physical Component Summary				Fusion Controls Physical Component Summary				*t* Test	Effect
	N	Mean	SD	Median	N	Mean	SD	Median	*P**	Size†
Preoperative	195	28.1	6.6	27.6	95	28.2	6.0	27.4	0.939	−0.02
Month 24	148	43.8	10.6	43.9	78	40.7	12.2	40.5	0.050	0.28
	Coflex Mental Health Summary				Fusion Controls Mental Health Summary				*t* test	Effect
	N	Mean	SD	Median	N	Mean	SD	Median	*P**	Size†
Preoperative	195	45.5	13.0	45.9	95	44.9	12.2	43.6	0.695	0.05
Month 24	148	53.3	10.2	57.8	78	51.2	11.3	56.8	0.150	0.20

**Two sample pooled t test P value.*

†Standardized effect size (group difference in means divided by pooled within group SD). Larger values of the PCS and MCS reflect greater health related quality of life. Therefore, positive effect sizes reflect improvements in group implanted with the investigational device relative to control.

SF-12 indicates Short-Form 12.

Table 9 shows that both superior and inferior adjacent level translation in the fusion cohort exhibited a trend toward a significant increase ($P = 0.087$, $P = 0.083$, respectively) compared with Coflex subjects at 24 months.

Overall Success (Primary Endpoint)

At 24 months, 135 of 204 Coflex subjects (66.2%) and 60 of 104 (57.7%) fusion controls met the criteria for overall study success, demonstrating noninferiority (posterior probability = 0.999).

Adverse Events and Secondary Surgical Procedures

The overall adverse event rates were similar between the groups, and there were no group differences with respect to any operative site adverse event (49.3% Coflex *vs*. 43.9% fusion), any adverse event definitely/probably related to the implant (13.5% Coflex *vs*. 18.7% fusion), or any adverse event definitely/probably related to the surgery (23.7% *vs*. 30.8%). The rate of spinous process fracture was 14.0% in the Coflex group, however, 48% of these had healed radiographically at 2 years. The presence of a spinous process fracture did not impact the clinical outcome because the vast majority was asymptomatic and identified by the core radiographical laboratory, not by the treating surgeon. The composite clinical success in the fracture group at 24 months was 76.7% compared with the no-fracture group (64.4%, $P = 0.216$).

From 0 to 24 months postoperatively, the reoperation rate for Coflex was 23/215 (10.7%) compared with 8 of

TABLE 6. Coflex and Fusion Control Randomized Cohorts Descriptive Statistics for Back and Max (Right, Left) Leg Pain VAS

	Coflex Back Pain VAS				Controls Back Pain VAS				*t* Test	Effect
	N	Mean	SD	Median	N	Mean	SD	Median	*P**	Size†
Preoperative	215	79.5	15.0	82.0	106	79.2	13.5	81.0	0.843	0.02
Month 24	162	23.6	26.2	12.0	86	27.0	29.3	13.0	0.345	−0.13
	Coflex Leg Pain (Worse Leg)				Controls Leg Pain (Worse Leg)				*t* Test	Effect
	N	Mean	SD	Median	N	Mean	SD	Median	*P**	Size†
Preoperative	215	76.0	20.4	80.0	106	78.3	18.4	82.5	0.307	−0.12
Month 24	162	20.6	27.4	7.0	86	24.1	30.6	8.0	0.364	−0.12

**Two sample pooled t test P value.*

†Standardized effect size (group difference in means divided by pooled within group SD). The VAS were anchored at 0 (No Pain) and 100 (Worst Possible Pain). Therefore, negative effect sizes reflect less pain in the group implanted with the investigational device relative to control. For analysis purposes, leg pain was defined as the maximum pain experienced in the right and left legs.

VAS indicates visual analogue scale scores; SD indicates standard deviation.

TABLE 7. Coflex and Fusion Control Randomized Cohorts Descriptive Statistics for the Zurich Claudication Questionnaire

	Coflex Symptom Severity				Fusion Control Symptom Severity				*t* Test	Effect
	N	Mean	SD	Median	N	Mean	SD	Median	*P**	Size†
Preoperative	214	3.56	0.61	3.57	107	3.58	0.57	3.43	0.680	−0.05
Month 24	161	1.98	0.75	1.86	86	2.23	0.89	2.29	0.023	−0.30
	Coflex Physical Function				Fusion Control Physical Function				*t* Test	Effect
	N	Mean	SD	Median	N	Mean	SD	Median	*P**	Size†
Preoperative	214	2.75	0.45	2.80	107	2.82	0.44	2.80	0.188	−0.16
Month 24	162	1.56	0.61	1.40	86	1.80	0.77	1.60	0.008	−0.35
	Coflex Satisfaction Score‡				Controls Satisfaction Score				*t* Test	Effect
	N	Mean	SD	Median	N	Mean	SD	Median	*P**	Size†
Month 24	162	1.42	0.55	1.17	86	1.65	0.77	1.33	0.006	−0.36

**Two sample pooled t test P value.*

†Standardized effect size (group difference in means divided by pooled within group SD). Smaller values of the satisfaction score reflect greater satisfaction. Therefore, negative effect sizes reflect greater satisfaction in the Coflex group compared with the control group.

‡The satisfaction score is not assessed at the preoperative evaluation.

SD indicates standard deviation.

107 for fusion (7.5%, $P = 0.426$). Among the 23 patients with reoperations within the Coflex group, there were 13 conversion to a primary lumbar fusion, 6 irrigation and debridements for wound-related issues (5 with retention of the device), and 6 revision decompressions (4 with device removal).

TABLE 8. Coflex and Fusion Control Randomized Cohort Flexion Extension-Rotation (F–E) (°)

	Coflex					Fusion Control					*t* Test
	At Level(s) of Implant (per Level)										
	N	Mean	SD	Min	Max	N	Mean	SD	Min	Max	*P**
Preoperative	281	4.55	3.86	0.00	19.30	145	4.15	3.33	0.10	15.50	0.286
Month 24	254	4.17	3.90	0.00	17.00	140	1.59	1.97	1.00	12.40	0.000
	Below Level of Implant (per Patient)										*t* Test
	N	Mean	SD	Min	Max	N	Mean	SD	Min	Max	*P**
Preoperative	195	5.81	4.14	0.00	18.10	101	5.65	3.84	0.00	18.10	0.750
Month 24	176	6.53	4.66	0.10	23.20	96	6.95	4.42	0.30	21.90	0.471
	Above Level of Implant (per Patient)										*t* test
	N	Mean	SD	Min	Max	N	Mean	SD	Min	Max	*P**
Preoperative	207	4.17	3.49	0.00	17.40	104	3.68	2.99	0.10	11.60	0.222
Month 24	186	4.08	3.57	0.10	18.20	102	5.60	4.62	0.10	18.60	0.002

**Two sample pooled t test P value.*

†Mean difference is Coflex mean minus fusion mean. 95% confidence interval is for the mean difference.

SD indicates standard deviation.

TABLE 9. Coflex and Fusion Control Randomized Cohort Flexion Extension-Translation (mm)

	Coflex					Fusion Control					
	At Level(s) of Implant (per Level)										*t* Test
	N	Mean	SD	Min	Max	N	Mean	SD	Min	Max	*P**
Preoperative	274	0.97	0.88	0.00	4.70	134	0.97	0.85	0.00	3.80	0.948
Month 24	251	0.93	0.89	0.00	5.60	130	0.39	0.50	0.00	2.70	0.000
	Below Level of Implant (per Patient)										*t* Test
	N	Mean	SD	Min	Max	N	Mean	SD	Min	Max	*P**
Preoperative	190	0.56	0.53	0.00	2.60	93	0.55	0.46	0.00	2.10	0.882
Month 24	174	0.65	0.57	0.00	3.80	89	0.80	0.85	0.00	5.10	0.083
	Above Level of Implant (per Patient)										*t* Test
	N	Mean	SD	Min	Max	N	Mean	SD	Min	Max	*P**
Preoperative	202	0.87	0.74	0.00	4.60	96	0.77	0.76	0.00	3.70	0.290
Month 24	184	0.89	0.82	0.00	4.30	95	1.08	0.94	0.00	4.30	0.087

**Two sample pooled t test P value.*

†Mean difference is Coflex mean minus fusion mean. 95% confidence interval is for the mean difference.

SD indicates standard deviation.

DISCUSSION

This study provides level 1 evidence from a randomized, prospective, multicenter FDA Investigational Device Exemption trial that laminectomy with Coflex interlaminar stabilization provided equivalent or superior outcomes to laminectomy and posterior spinal fusion in the treatment of spinal stenosis and degenerative spondylolisthesis. Our study is the first to demonstrate equivalence or superiority with a nonfusion device compared with the "gold standard" lumbar fusion in the treatment of patients with spinal stenosis and low back pain or degenerative spondylolisthesis.

Although our study met the FDA-determined *a priori* success criteria of noninferiority compared with fusion controls, with a similar safety profile and adverse event rate, the Coflex interlaminar device significantly outperformed fusion controls in several notable outcomes, which highlights several distinct advantages of Coflex stabilization compared with fusion. First, perioperative outcomes (hospital LOS, estimated blood loss, and operative times) were significantly reduced with Coflex. On average, for 1-level procedures the average hospital LOS with the Coflex cohort was 1.14 days shorter than fusion, while for 2-level procedures the difference was 1.99 days. In combination with reduced operative times, the data and literature suggest that there is the potential for reduced resource use and cost savings with Coflex while still achieving the same or better clinical results.[32]

A second potential advantage of Coflex compared with fusion is seen in the significantly improved functional and clinical outcomes. At multiple early postoperative time points, the Coflex cohort experienced improved outcomes with respect to ODI, with significance achieved early and 24-month improvements seen in all 3 sub domains of ZCQ, and SF-12 Physical Component. This is most likely attributable to the less-invasive nature of Coflex implantation after laminectomy, which incurs less surgical dissection, less blood loss, and may explain the reduced early postoperative pain profile compared with fusion. In contrast to lumbar fusion, Coflex device implantation does not require any further surgical dissection to expose the facet joints or the transverse processes. Others have similarly reported improved early clinical outcomes with less-invasive procedures due to less tissue damage, blood loss, and postoperative pain.[33,34]

Radiographical evaluation at the adjacent levels at 2 years suggests that the Coflex device allows for maintenance of physiological motion, while fusions experienced increased angular range of motion and translation at the superior adjacent level. Longer-term data is required to demonstrate whether or not motion preservation with the Coflex device will lead to lower reoperation rates for adjacent level disease compared with fusion surgery.

Similar to the findings from Weinstein *et al*[3] from the SPORT studies, our results demonstrate significant improvements with surgical treatment from baseline in both the spinal stenosis and degenerative spondylolisthesis populations at 2 years.[35] In the degenerative spondylolisthesis SPORT study cohort, ODI scores in the surgically-treated randomized group improved by 24.2 points from 45.0 to 20.8 at 2 years. Similarly, in patients with spinal stenosis without spondylolisthesis, Weinstein *et al*[3] reported improvement in ODI scores of 20.3 points from 43.2 to 22.9 at 2 years. In this

study, the Coflex cohort (in the treatment of both degenerative spondylolisthesis and in stenosis without slip) demonstrated improvement of by 38.8 points from 60.8 at baseline to 22.0 at 2 years, while the fusion cohort improved by 34 points from 60.7 at baseline to 26.7 at 2 years. Our results also compare favorably with the data recently reported from Pearson *et al*[12] and the SPORT study who showed that among the cohort of patients with predominant back pain, ODI scores improved at 2 years by 20.3 points in patients with degenerative spondylolisthesis and 16.4 points in the spinal stenosis cohorts, significantly lower than patients with predominant leg pain (29.6 and 25.4 points, respectively).

Reoperation rates among the SPORT studies l for stenosis with and without spondylolisthesis was in the range of 7% to 12% at 2 years, which is similar to the secondary surgery rate for the Coflex cohort at 2 years of 10.7%.[3,35] The rate of reoperation was higher in the Coflex cohort compared with fusion, although the difference was not statistically significant. For the 13 patients who required Coflex device removal and conversion to fusion, these subjects ultimately received the procedure (primary lumbar fusion) that they would otherwise have received if the Coflex device were not available. In this cohort that ultimately received Coflex removal and lumbar spinal fusion, the Coflex device acted as a bridge between conservative treatment and fusion, while for 202 of 215 (94%) of patients, Coflex served as the definitive treatment.

There are notable limitations to the Coflex device. Patients with grade 2 spondylolisthesis are not candidates for Coflex stabilization as the device is not intended to treat these larger instabilities. As the Coflex device is placed into the interlaminar space, there exists the potential for spinous process fracture. However, the presence of a fracture did not impact the clinical outcome and were identified most often by the core radiographical laboratory on CT scan as part of the standard postoperative radiographical study protocol, not the treating physician. Finally, patients with osteopenia or osteoporosis should not receive the device due to the potential for increased risk of spinous process fractures.

The primary study limitation is the potential for patient expectation bias that may result from the patients not being blinded to the treatment received postoperatively. In the optimal study design, patients would be blinded to the treatment received postoperatively, a study feature not feasible in the current study design. Another potential study limitation is that a subset of patients with stenosis and stable spondylolisthesis, without significant back pain, may benefit from decompression alone without stabilization; however, this group was not the focus of this study, as low back pain was a stringent requirement for inclusion into the study. A third limitation is that due to insufficient numbers available, a comparison of retrolisthesis *versus* anterolisthesis was not possible, but should be examined in future studies with larger numbers available. Finally, the fusion control group did not include bone morphogenetic protein or intervertebral cages, which were not used in this study, as their use is not considered on label for the treatment of spinal stenosis.

CONCLUSION

In conclusion, the current data demonstrate that Coflex interlaminar stabilization after laminectomy is a viable alternative to lumbar spinal fusion. Advantages in perioperative outcomes, and equivalent or superior 2-year clinical outcomes data were seen with Coflex, while the clinical relevance, if any, of maintained operative and adjacent level motion will need to be studied when longer-term follow-up is available. The safety profile and adverse event rates are similar, with secondary surgery rates that are equivalent to that of fusion reported in the literature, but are higher in the Coflex cohort at 2 years, although this difference did not achieve statistical significance.[4,16] We conclude that Coflex interlaminar stabilization is a safe, efficacious, and viable alternative to spinal fusion and an adjunct to laminectomy in the treatment of spinal stenosis with low back pain and degenerative spondylolisthesis.

➢ Key Points

- ❑ Coflex interlaminar stabilization led to shorter surgical times, reduced hospital LOS, and less blood loss compared with instrumented spinal fusion for lumbar spinal stenosis with up to grade 1 degenerative spondylolisthesis.
- ❑ At 24 months, significant improvements were seen in the Coflex cohort compared with fusion in all ZCQ subdomains, SF-12 Physical Component, and a trend toward significance was seen in ODI.
- ❑ Fusions exhibited significantly increased angulation at the superior adjacent level, and a trend toward significant increase in superior level translation, at 2 years, compared with Coflex interlaminar stabilization.
- ❑ Based on the strict FDA criteria for overall success, Coflex succeeded in 66.2% of patients, compared with 57.7% of fusions at 2 years, demonstrating noninferiority.

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