Randomized Trial

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Superion Interspinous Process Spacer for Intermittent Neurogenic Claudication Secondary to Moderate Lumbar Spinal Stenosis

Two-Year Results From a Randomized Controlled FDA-IDE Pivotal Trial

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**Study Design.** Prospective, multicenter, randomized, controlled, investigational device exemption noninferiority trial.

**Objective.** To determine 2-year outcomes in patients with intermittent neurogenic claudication secondary to moderate lumbar spinal stenosis (LSS) who were treated with the Superion interspinous process spacer.

**Summary of Background Data.** Interspinous spacers are a less-invasive treatment alternative compared with surgical decompression for patients with LSS unresponsive to conservative care. High-quality comparative data with these devices are lacking.

**Methods.** Patients presenting with intermittent neurogenic claudication secondary to moderate LSS who failed at least 6 months of nonsurgical management were randomly allocated to treatment with the Superion spacer or a control spacer (X-Stop) and followed for 2 years.

**Results.** A total of 391 randomized patients were implanted with Superion (n = 190) or control (n = 201) spacers at 29 sites in the United States between August 2008 and December 2011. Implants were successfully implanted in 99.5% of patients with Superion and 99.0% of control patients. The primary composite endpoint of this study was met, which demonstrated that the Superion spacer was noninferior to the X-Stop spacer. Leg pain, the predominant patient complaint, decreased in severity by 70% during 2 years in each group. Most (77%) patients achieved leg pain clinical success (improvement ≥20 mm) at 2 years. Back pain clinical success (improvement ≥20 mm) was 68%, with no differences between groups. Oswestry Disability Index clinical success (≥15% point improvement) was achieved in 65% of patients. The rates of complications and reoperations were similar between groups.

**Conclusion.** The Superion interspinous process spacer relieves symptoms of intermittent neurogenic claudication secondary to moderate LSS in the majority of patients through 2 years.

**Key words:** implant, indirect decompression, intermittent neurogenic claudication, interspinous process spacer, lumbar spinal stenosis, randomized controlled trial, Superion.

**Level of Evidence:** 2

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Lumbar spinal stenosis (LSS) with intermittent neurogenic claudication represents a challenging therapeutic dilemma. Interspinous process spacers are a less-invasive alternative to surgical decompression in patients who have failed nonsurgical management. The mechanism of action is thought to be distraction of the spinous processes and/or limiting extension of the lumbar spine, which lessens the mechanically induced stenosis associated with lumbar extension, thus relieving claudicatory symptoms. In 2005, the X-Stop Interspinous Process Decompression System (Medtronic Inc., Minneapolis, MN) became the first Food and Drug Administration (FDA)-approved interspinous process spacer for treatment of neurogenic claudication secondary to LSS. Since
The Superion interspinous process spacer (Vertiflex Inc., San Clemente, CA) was designed to be implanted between contiguous spinous processes via a less-invasive approach compared with the X-Stop spacer. The purpose of this randomized controlled trial was to compare 2-year outcomes in patients with intermittent neurogenic claudication secondary to moderate LSS who were treated with the Superion spacer or a control spacer (X-Stop).

**MATERIALS AND METHODS**

**Ethics**

This was a prospective, multicenter, randomized, controlled investigational device exemption trial approved by the United States FDA. This study was approved by the institutional review board at each participating site and patients provided written informed consent before any study-related procedures were performed. The trial was prospectively registered at ClinicalTrials.gov (NCT00692276).

**Patients**

Patients presenting with neurogenic intermittent claudication symptoms were screened for study eligibility. Eligible patients were at least 45 years of age and reported symptoms of intermittent neurogenic claudication secondary to a confirmed diagnosis of LSS at 1 or 2 contiguous levels from L1 to L5, despite at least 6 months of nonsurgical management. Key study inclusion and exclusion criteria are provided in Table, Supplemental Digital Content 1 available at http://links.lww.com/BRS/A948.

**Procedures**

Pretreatment evaluations included a physical and neurological examination, medical history, and assessment for study eligibility based on predefined inclusion/exclusion criteria. Radiographical assessments included radiographs (standing anteroposterior, lateral, and flexion/extension lateral lumbar) and magnetic resonance images or computed tomographic scans of the lumbar spine.

The Superion interspinous process spacer (Figures 1, 2) is a titanium implant delivered through a cannula and deployed between the spinous processes of the involved vertebral levels. The device consists of an implant body and 2 cam lobes that rotate during deployment to encompass the lateral aspects of the superior and inferior spinous processes. Device sizes range from 8 to 16 mm, with each size corresponding to the magnitude of desired distraction between the 2 spinous processes (Figure 3). Comprehensive descriptions of the Superion and X-Stop interspinous process spacers and operative technique have been previously reported.

**Outcomes**

Subjects were followed through hospital discharge and returned for visits at 6 weeks and 3, 6, 12, 18, and 24 months. A physical and neurological assessment was performed at all follow-up visits; neurological success was defined by freedom from new or worsening motor or sensory function. Radiographical evaluations included standing anteroposterior, lateral, and flexion/extension lateral lumbar radiographs. The primary endpoint of this study was a composite treatment success outcome at the 2-year follow-up visit, defined as: (1) clinically significant improvement in at least 2 of 3 Zurich Claudication Questionnaire (ZCQ) domain scores compared with baseline (physical function ≥0.5-point decrease, symptom severity ≥0.5-point decrease, patient satisfaction score <2.5), (2) freedom from reoperation, revision, removal, or supplemental fixation at the index level, (3) freedom from epidural steroid injection or nerve block at the index level within 12 weeks of the 2-year visit, (4) freedom from rhizotomy or spinal cord stimulator at any level, and (5) freedom from major implant or procedure-related complications. Secondary outcomes included leg and back pain severity assessed on a 100-mm visual analogue scale, Oswestry Disability Index (version 2), patient satisfaction questions rated on a 5-point Likert scale ranging from very satisfied to very dissatisfied, radiographical evaluations, and adverse events classified by seriousness and relationship to the device and/or procedure.

**Hypotheses**

The primary hypothesis was that the composite treatment success outcome at 2 years in patients treated with Superion would be noninferior to that of patients treated with X-Stop. A noninferiority margin of 10% was determined...
to be a clinically nonsignificant difference. Using a Bayesian approach, noninferiority would be claimed if the posterior probability of the null hypothesis was 95.8% or more, a value that was selected to ensure that the type I error remained less than 0.05.

Sample Size
A prospectively defined Bayesian adaptive sample size approach was used, which specified a total evaluable sample size ranging from 250 to 350 patients. An interim analysis was scheduled when patient accrual reached 250, 300, and 350. At each interim period, patient enrollment was either scheduled to stop if trial success was determined (posterior probability of the null hypothesis ≥95.8%) or continue to the next planned interim analysis, up to a maximum of 350 patients.

Randomization and Blinding
Patients were randomly allocated (1:1) to implant with Superion or X-Stop interspinous spacers and stratified by sex and number of index levels at each site. A web-based electronic data capture system was used to obtain treatment assignment before each patient was enrolled. Treatments were not concealed to investigators, outcome assessors, or trial participants.

Data Quality
This clinical trial was conducted per Good Clinical Practice guidance. Prior to commencing any study activity at any site, each investigator was trained in Good Clinical Practice, the study protocol, and the surgical technique for both interspinous process spacers. Data were regularly monitored by the sponsor and an independent contract research organization. Electronic data capture was handled by an independent firm (MedNet Solutions, Minnetonka, MN). A core radiographical laboratory (Medical Metrics Inc., Houston, TX) independently reviewed radiographs for evidence of spinous process fracture, and device disassembly, dislodgement, or migration.

Statistical Methods
Statistical analysis was performed by independent biostatisticians, who received all data for analysis directly from the electronic database. All outcomes were reported using a modified intent-to-treat population, which included all randomized patients who began anesthesia on the implant date. Continuous data were reported as mean ± standard deviation and categorical data were reported as frequencies and percentages. Comparisons of baseline characteristics were performed with independent samples t test, the Wilcoxon signed rank test, or Fisher exact test, as appropriate. Longitudinal changes in clinical outcomes between groups were assessed with unpaired t tests. Minimal clinically important changes in symptom severity were defined as 20-mm or more improvement in pain scores and a 15%-point or more improvement in Oswestry Disability Index. The Kaplan-Meier method and log-rank tests were used to analyze freedom from reoperation through 2 years. The primary endpoint was assessed using a Bayesian approach that specified a posterior probability of the null hypothesis at 95.8% or more. Details of the Bayesian methodology were specified in a separate statistical analysis plan.

RESULTS
Participant Flow and Accountability
A total of 440 patients were randomized at 29 sites between August 2008 and December 2011 (Figure, Supplemental Digital Content 2 available at http://links.lww.com/BRS/A948). A total of 49 patients (Superion 28, control 21) were discontinued before treatment, most commonly due to withdrawal of informed consent. Ultimately, 391 were implanted with Superion (n = 190) or control (n = 201) spacers. During the 2-year follow-up period, 111 patients (Superion 54, control 57) were withdrawn from the study due to a protocol-defined secondary intervention, including device explant, revision surgery at the index level without explant, rhizotomy, rehospitalization for deep infection, or lumbar injection at the index
level. Of the remaining patients, follow-up visit compliance was excellent (Superion 96.7%, control 94.7%).

**Subject Characteristics**
Baseline patient characteristics, including demographics, medical history, and symptom severity, were comparable between groups (Table 1). Only one baseline characteristic (ZCQ Physical Function) was statistically different between groups although this was not deemed a clinically important difference. Baseline radiographical findings are shown in Table, Supplemental Digital Content 3 available at http://links.lww.com/BRS/A948. Spinal stenosis was most frequently identified at L3–L4 or L4–L5. The incidence of low-grade spondylolisthesis was 32% at L4–L5, 9% at L3–L4, 1% at L2–L3, and 0% at L1–L2.

**Operative Details**
Interspinous process spacer implant success was 99.5% with Superion and 99.0% with control. Approximately 50% of patients were implanted at 1-level (typically L4–L5) and 50% at 2 levels (typically L3–L4/L4–L5). An important distinction between devices is that the X-Stop requires an open surgical procedure.
approach, whereas access is gained percutaneously (47%) or with a miniopen incision (53%) with the Superion spacer (Table 2). Blood loss (median: 5 vs. 25 mL, \( P < 0.001 \)) and hospital stay (median: 1 vs. 2 days, \( P < 0.05 \)) favored patients treated with Superion.

**Primary Endpoint: Composite Treatment Success Outcome**

Using a Bayesian approach, the posterior probability that the composite treatment success outcome through 2 years with Superion was no less than the 10% noninferiority margin compared with X-Stop was 0.993. This posterior probability exceeded the *a priori* criterion of 0.958, providing evidence that Superion is clinically noninferior to X-Stop. A number of sensitivity analyses were performed that corroborated the findings of the primary analysis. A tipping point analysis confirmed that the Bayesian posterior probability exceeded 0.958 in 92% of simulations.

**Patient-Reported Symptoms**

Leg pain severity decreased by 70% in both the Superion and control groups, with mean values of 20 ± 30 and 20 ± 26 at 2 years, respectively (Figure 4). At 2 years, leg pain clinical success was 76% with Superion and 77% with control. Back pain severity decreased by 65% in the Superion group and 69% with the control spacer, with mean values of 20 ± 26 and 18 ± 23 at 2 years, respectively (Figure 5). At 2 years, back pain clinical success was comparable (Superion 67%, control 68%, \( P = 0.90 \)). Back-specific disability improved 51% with the Superion and 55% with the control spacer, with mean values of 20 ± 18 and 18 ± 15 at 2 years, respectively (Figure 6). At 2 years, Oswestry Disability Index clinical success was 63% with Superion and 67% with control (\( P = 0.61 \)). ZCQ subdomain scores through 2 years were comparable between groups (Figure, Supplemental Digital Content 4 available at http://links.lww.com/BRS/A948). For symptom severity, mean improvement was 1.15 for Superion and 1.28 points for control. At 2 years, mean ZCQ Patient Satisfaction scores were also comparable (Superion, 1.66; control, 1.52). Overall, patient-reported outcomes at 2 years were comparable in patients with and without spondylolisthesis (Table 3) and in patients with central versus lateral stenosis (Table 4).

**Patient Satisfaction**

The percentage of patients who were “satisfied” or “somewhat satisfied” with their treatment at 2 years was 86% with Superion and 89% with control. Similarly, 83% and 84% of patients, respectively, reported that they would “definitely” or “probably” undergo the same treatment again.

**Radiographical Findings**

There were no instances of device component fracture, disassembly, or collapse in either group as reported by independent radiographical assessment. Device dislodgement or
migration was identified in 0% of patients with Superion and 11.9% of control patients. At 2 years, the incidence of nonhealed spinous process fracture was 11.1% with Superion and 5.0% with the control spacer; healed spinous process fracture incidence was 5.3% with Superion and 3.5% in the control group. Approximately, 80% of spinous process fractures were identified by the 6-week follow-up visit in each group. Spinous process fractures were largely asymptomatic and had no influence on clinical effectiveness of either device.

Reoperations
There were a total of 44 (23.2%) reoperations or revisions in the Superion group compared with 38 (18.9%) in the control group ($P = 0.32$). Similar rates of decompression and device removal (11.6% Superion vs. 9.5% control, $P = 0.51$) and device removal and fusion (6.8% Superion vs. 5.5% control, $P = 0.68$) were observed. Comparing Superion to control, the frequency of other interventions was 0.5% versus 1.0% for device removal, 2.1% versus 0.0% for supplemental decompression, and 0.5% versus 1.0% for intraoperative complication preventing implantation. No patient was treated with a spinal cord stimulator at the index level and only 1 patient (control) received rhizotomy. During the 2-year follow-up period, 13.2% of patients with Superion and 16.4% of control patients received an epidural steroid injection or nerve block at the level(s) of surgery ($P = 0.40$). The Kaplan-Meier estimate of freedom from reoperation, revision, or epidural injection through 2 years was 72% (Figure 7). The main reasons for reoperation in each group were inadequate pain relief or return of symptoms.

Adverse Events
The incidence of adverse events was similar between the groups (Table 5). The incidence of serious adverse events classified as device or procedure-related was 8.4% with Superion and 9.5% with control ($P = 0.86$). Through 2 years, 6 (3.2%) deaths were reported in the Superion group and 5 (2.5%) in the control group ($P = 0.77$). No device- or procedure-related deaths were reported during follow-up. The rate of neurological complications was similar for both Superion (3.7%) and control (2.5%) groups.

DISCUSSION
The results of this randomized controlled trial demonstrate that the Superion interspinous process spacer provides
clinically meaningful relief of intermittent claudication symptoms due to LSS through 2 years. Furthermore, patient outcomes were comparable with those observed with the X-Stop, an FDA-approved interspinous spacer. The primary endpoint of this clinical trial was met, demonstrating noninferiority of the Superion spacer compared with the X-Stop spacer.

Despite the similarities in mechanism of action as well as clinical and radiographical outcomes, there are distinct differences in device design and surgical placement technique between these spacers that warrant further discussion. Both devices are inserted through a posterior incision and require initial distraction. However, the X-Stop requires much greater surgical exposure whereas the Superion device uses a minimally invasive approach, such that the device is inserted through a cannula about the size of a dime placed between adjacent spinous processes and, therefore, requires no surgical dissection of the spinal musculature. We attribute the smaller blood loss and shorter hospital stay associated with Superion to these procedural differences. The minimally invasive nature of the Superion spacer is also advantageous compared with the larger incision required for the control spacer in patients who later require secondary surgery because larger exposures generate scar tissue, making future reoperations more difficult.

In addition to the operative benefits, there are also biomechanical characteristics that may favor the Superion device. On the basis of the radiographical data, there were a significant number of dislodgements and migrations with the X-Stop device whereas none were observed in the Superion group. These events may occur because the open procedure results in greater disruption of anatomic structures, which may lead to a greater propensity for the X-Stop to dislodge or migrate. In addition, the slender wings of the X-Stop device may provide less stability between the spinous processes. The patients with dislodgements in the X-Stop group not only exhibited greater pain and loss of function, but also required a higher rate of additional surgical procedures.

In this study, the core laboratory also identified spinous process fractures in both groups. Most fractures were asymptomatic and the adverse event rate associated with spinous process fractures was not significantly higher than in patients without fractures. The long-term significance of these fractures is unknown; however, radiographical follow-up suggests healing is common. Potentially, spinous process fracture risk can be lowered by bone density screening to identify individuals with osteoporosis, exclusion of patients with high-grade spondylolisthesis deformities, accurate device sizing, proper patient positioning, and avoidance of overdistraction of the interspinous space.

Data from this investigation as well as from previous studies suggest that the midterm treatment effectiveness of interspinous spacers is at least comparable with that of open decompression surgery. Leg pain, which is the primary complaint in this patient population, decreased by approximately 70% during 2 years in this study. According to published literature, leg pain severity generally decreases by 43% to 69% after laminectomy. Furthermore, interspinous spacers are appealing to patients because of the less-invasive nature of this procedure relative to surgical decompression. For example, in the Spine Patient Outcomes Research Trial trial,18 procedural outcomes included blood loss more than 300 mL, procedure time more than 2 hours, and hospitalization more than 3 days. In contrast, interspinous spacers result in minimal blood loss (5–25 mL) with reductions in procedure time and hospital stay of approximately 50%. Regardless, proper patient selection, meticulous surgical technique, and familiarity with relevant anatomy are prerequisites for favorable outcomes with interspinous process spacers.

Despite the strengths of this study that include a randomized design with rigorous study entry criteria and excellent patient follow-up rates using validated outcome measures, there were several limitations. The long-term durability of interspinous

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**Figure 7.** Freedom from reoperation, reintervention, and epidural through 2 years.

**TABLE 5. Adverse Events Through 2 Years**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Superion (n = 190)</th>
<th>X-Stop (n = 201)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any adverse event, n (%)</td>
<td>180 (94.7)</td>
<td>184 (91.5)</td>
<td>0.24</td>
</tr>
<tr>
<td>Back pain</td>
<td>49 (25.8)</td>
<td>61 (30.3)</td>
<td></td>
</tr>
<tr>
<td>Leg pain</td>
<td>33 (17.4)</td>
<td>45 (22.4)</td>
<td></td>
</tr>
<tr>
<td>LSS symptoms at index level</td>
<td>26 (13.7)</td>
<td>28 (13.9)</td>
<td></td>
</tr>
<tr>
<td>Spinal process fracture</td>
<td>23 (12.1)</td>
<td>13 (6.5)</td>
<td></td>
</tr>
<tr>
<td>Buttock/groin pain</td>
<td>19 (10.0)</td>
<td>12 (6.0)</td>
<td></td>
</tr>
<tr>
<td>Any serious adverse event, n (%)</td>
<td>88 (46.3)</td>
<td>92 (45.8)</td>
<td>0.92</td>
</tr>
<tr>
<td>LSS symptoms at index level</td>
<td>16 (8.4)</td>
<td>13 (6.5)</td>
<td></td>
</tr>
<tr>
<td>Leg pain</td>
<td>11 (5.8)</td>
<td>10 (5.0)</td>
<td></td>
</tr>
<tr>
<td>Spinal process fracture</td>
<td>10 (5.3)</td>
<td>5 (2.5)</td>
<td></td>
</tr>
<tr>
<td>Back pain</td>
<td>8 (4.2)</td>
<td>13 (6.5)</td>
<td></td>
</tr>
</tbody>
</table>

Adverse events reported with frequency more than 5% in either group. LSS indicates lumbar spinal stenosis.
process spacers is currently unknown and requires further investigation. In addition, the generalizability of these findings may only be applicable to patients with radiographically confirmed moderate LSS with no more than low-grade spondylolisthesis deformities. The finding that patients with a spinous process fracture yielded similar long-term clinical results to patients without a spinous process fracture brings into question the mechanisms of mechanical action of these devices. Finally, a comparison of interspinous process spacers with nonsurgical treatment or surgical decompression was not performed so this randomized study provides no information on these interesting questions.

CONCLUSION
The Superion and X-Stop interspinous process spacers both relieve symptoms of intermittent neurogenic claudication secondary to moderate LSS. In addition, the safety profiles of these devices were comparable. The Superion device may represent a reasonable treatment option for this patient population.

Key Points
- A total of 391 patients with moderate LSS who failed at least 6 months of nonsurgical management were treated with the Superion (n = 190) or a control (n = 201) interspinous process spacer as part of a multicenter, randomized, controlled trial.
- During 2 years, the implantation of an interspinous spacer resulted in a 70% reduction in leg pain severity with high patient satisfaction.
- The Superion interspinous process spacer relieves symptoms of intermittent neurogenic claudication secondary to moderate LSS in the majority of patients through 2 years.

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References