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Minimally invasive lumbar decompression: a review of indications, techniques, efficacy and safety

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Practice points

- Neurogenic claudication due to lumbar spinal stenosis presents most commonly as gluteal or leg pain with walking or standing that is alleviated with sitting.
- A major cause of lumbar spinal stenosis is ligamentum flavum hypertrophy (LFH), which contributes up to 85% of spinal canal narrowing.
- The *mild*® procedure debulks LFH with a goal of relieving symptoms of neurogenic claudication.
- Patients with LFH and multiple other spinal comorbidities, including lateral and foraminal stenosis, have shown significant improvement in mobility and pain after the *mild* procedure.
- *mild* candidates must present with neurogenic claudication, and stenosis must be confirmed on imaging with ligamentum flavum ≥ 2.5 mm.
- The *mild* procedure is performed percutaneously through a 5.1-mm port with specially designed minimally invasive instruments and can be done unilaterally or bilaterally, and at multiple levels, leaving no implants behind.
- *mild* has been shown to be as safe as an epidural steroid injection.
- Following treatment with *mild*, patients typically resume normal activity within 24 h with no restrictions.
- Thirteen clinical studies, including two level 1 randomized controlled trials, have demonstrated statistically significant improvement in pain and mobility, and superiority of *mild* versus epidural steroid injections.

Lumbar spinal stenosis is a common degenerative spine condition. In properly selected patients, minimally invasive lumbar decompression (*mild*®) may be an option to improve outcomes. This review provides an in-depth description of the *mild* procedure and a comprehensive examination of safety and efficacy. Two randomized controlled trials, together with 11 other controlled clinical studies, have established the efficacy of *mild*, which is a minimally invasive procedure that does not involve implants and has demonstrated excellent efficacy and safety. With an established safety profile equivalent to epidural steroid injections, and efficacy that has been shown to be superior to such injections, *mild* can reasonably be positioned early in the treatment algorithm for these patients. Based on extensive review of the literature, robust safety and efficacy through 2 years, and in accordance with minimally invasive spine treatment guidelines, *mild* is recommended as the first intervention after failure of conservative measures for lumbar spinal stenosis patients with neurogenic claudication and ligamentum flavum hypertrophy.

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Future
Medicine

Lumbar spinal stenosis (LSS) is a common degenerative spinal condition causing significant pain and functional disability, especially in the elderly. In 1976, Arnoldi *et al.* first defined LSS as any type of narrowing of the spinal canal, nerve root canals or intervertebral foramina [1]. The North American Spine Society clinical guideline development group has now defined LSS as “*a condition in which there is diminished space available for the neural and vascular elements in the lumbar spine secondary to degenerative changes in the spinal canal*” [2]. LSS may be congenital in nature or may be acquired over the years secondary to degenerative spine disease. Anteriorly, disc degeneration is a common cause, whereas posterior to the spinal canal, facet arthropathy and ligamentum flavum hypertrophy (LFH) are contributing causes of spinal stenosis. The prevalence of acquired LSS is estimated to be around 4% of the population under the age of 40 years old; however, it increases to approximately 19.4% in the 60–69-year-old age group [3]. Even though most LSS sufferers are asymptomatic, 10% of the population develop symptoms related to LSS by the age of 70 years old [4]. When symptomatic, LSS manifests itself with a constellation of clinical symptoms characterized by neurogenic claudication. The most common presentation of neurogenic claudication includes gluteal and/or leg pain, numbness, weakness, or fatigue with walking or standing that is alleviated with sitting and/or lumbar flexion [5].

Historically, definitive treatment of spinal stenosis has been decompressive surgery, which exposes patients to complications, extensive recovery periods and an economic healthcare burden. Conservative measures have been trialed, including physical therapy, NSAIDs and other pharmacological agents including calcitonin and prostaglandin E1 derivatives with limited benefit [6]. Epidural steroid injections (ESIs) may provide some symptomatic relief for a short period of time; however, this treatment modality has shown to be ineffective in treating patients with neurogenic claudication over a longer follow-up period [7,8]. Spinal cord stimulation is another treatment modality that has been attempted for the treatment of spinal stenosis, but it lacks robust evidence in favor of its use. Over the past decade, more minimally invasive therapies for the treatment of spinal stenosis have been assessed and corroborated by prospective, randomized trials. These include percutaneous image-guided lumbar decompression (PILD) and interspinous spacers [9].

This review will focus on the only commercially available PILD treatment option – *mild*® (minimally invasive lumbar decompression, Vertos Medical, CA, USA), a technique developed for the treatment of central stenosis of the lumbar region secondary to LFH. Preprocedural considerations, the technique, scientific evidence and comparative safety to other treatment modalities are described.

Ligamentum flavum hypertrophy

The ligamentum flavum (LF) is a thick ligament connecting the adjacent vertebrae from C2 to S1. It is a well-defined elastic structure that consists of elastic (80%) and collagen (20%) fibers [10]. The high elastic fiber content imparts its yellow color and is also referred to as the yellow ligament. However, with consistent wear and tear, LF becomes hypertrophied and results in lumbar spinal canal stenosis (LSCS) and its associated symptoms. This phenomenon was first described by Elsberg in 1913 [11]. Since then, LFH has been identified as a major cause of LSCS and can contribute to between 50 and 85% of spinal canal narrowing [12].

Pathogenesis

Hypertrophy and fibrosis of the LF has been attributed to the aging process and mechanical stress endured by the spine; however, the exact pathogenesis of LFH is still unknown. Yong-Hing *et al.* noted that the normal LF consists of 80% elastic fibers and 20% collagen fibers, but in spondylotic specimens, the content varies from 50 to 80% elastin and 20 to 50% collagen [13]. Multiple theories have been proposed to account for this phenomenon. Chen *et al.* reported results from their study documenting upregulation of *miR-155* in patients with LFH, which increased the expression of types I and III collagen in fibroblasts from LF [14]. Honsawek *et al.* demonstrated a correlation between LFH and greater bFGF expression but failed to establish causation [15]. In recent years, the role of TGF- β 1 has been suggested [16,17]. Another popular opinion is that angiogenesis represents a key step in the pathogenesis that follows mechanical stress during LFH development, and VEGF may play an important part in this process [18].

Figure 1. Axial cross-section of spinal cord depicting ligamentum flavum hypertrophy. (A) LF thickness (AP) measured perpendicular to the border of the lamina corresponding to the intervertebral disc. (B) MRI cross-sectional image demonstrating LSCS. Arrow demonstrates LFH measurement.

Diagnosis

Currently, magnetic resonance imaging (MRI), computed tomography (CT) and CT myelography are predominantly used for the diagnosis of LFH. MRI is the most commonly used modality due to its capability of yielding soft tissue contrast. CT and CT myelography may be utilized when there is a contraindication to performing MRI [19,20]. Although plain radiographs do not offer value in identifying LFH, they are an important tool in the assessment of spinal alignment and diagnosis of spondylolisthesis.

LF thickening is measured perpendicular to the border of the lamina corresponding to the intervertebral disc (Figure 1). The LF is hypertrophied if the thickness is ≥ 2.5 mm. However, the thickness of the LF does not correlate with the patient being symptomatic [21]. LF thickening is most commonly seen at L3–4 and L4–5 levels; more so than at L5–S1. LFH primarily results in central, foraminal and lateral recess stenosis.

Minimally invasive lumbar decompression: *mild*

History of the procedure

The *mild* procedure was developed by Dr David Solsberg and Dr Donald Schomer in 2005 as a system to help treat cancer patients who developed spinal stenosis but were not able to tolerate spine surgery secondary to comorbidities. It was originally named the X-Sten *mild* Tool Kit and received 510(k) clearance from the US FDA on 19 December 2006. The first patient was treated immediately following FDA clearance. Within a few years of its introduction, 12 clinical studies were completed that demonstrated the efficacy of the procedure. In 2016, 1-year results of the MiDAS ENCORE randomized controlled trial (RCT) reported that *mild* was statistically superior to ESIs in the treatment of select LSS patients. Following publication of this level 1 evidence, the US Centers for Medicare and Medicaid Services approved nationwide Medicare coverage of *mild* in 2017 [22].

Preoperative considerations & patient selection

To determine patient candidacy for the *mild* procedure, it is important to establish the diagnosis and etiology of LSS. History and physical examination of the patient establishes the diagnosis of symptomatic LSS, and etiology is primarily confirmed with imaging modalities. The most consistent finding of symptomatic spinal stenosis is the presence of neurogenic claudication, which includes little or no pain at rest and when sitting or lying in a recumbent position. However, upon standing or walking, these patients experience progressive back, buttock and/or

leg pain that may have a neuropathic (numbness and tingling) and mechanical (aching) component. This pain typically resolves within a short time after sitting or lying down.

Medical history is typically more sensitive than physical examination in determining the presence of LSS. Physical examination, including motor, sensory and reflex testing, is usually normal in such patients. Certain physical examination findings may be present in some patients, such as loss of normal lumbar lordosis that becomes evident if patients walk in a forward flexed position. The most common motor finding in LSS is weakness in L5 distribution (extensor hallucis longus), although asymmetric reflexes at the knee and ankle may also be present.

Once medical history and physical examination findings are suggestive of LSS, appropriate imaging is obtained to confirm the diagnosis and etiology of stenosis. MRI of the lumbar spine is the recommended imaging modality for such patients. If MRI is contraindicated, CT myelography/CT may also be used. The most common cut-off point for central canal stenosis is an anteroposterior (AP) diameter of the central canal <10 mm and/or cross-sectional area <100 mm² [23].

Suggested criteria for lateral stenosis include lateral recess height <2 mm and lateral recess depth <2 – 3 mm. Once the presence of stenosis is confirmed, its etiology must also be established. Only when LFH (LF ≥ 2.5 mm) is determined to be one of the causes of stenosis is the patient a candidate for the *mild* procedure. Spinal instability may also be assessed on imaging as open decompression/fusion is recommended in the presence of spondylolisthesis greater than grade II. Flexion/extension radiographs may be helpful in assessing spinal instability in such patients.

To summarize, all of the following inclusion criteria must be met for the patient to be a candidate for the *mild* procedure:

- Symptomatic LSS (i.e., presence of neurogenic claudication);
- Confirmation of stenosis on imaging;
- LFH (LF ≥ 2.5 mm).

The following contraindications must be accounted for before the procedure is performed on the patient:

Absolute contraindications:

- Prior spine surgery at the intended level of treatment;
- Presence of localized site of infection at the site of procedure.

Relative contraindications:

- Presence of higher than grade II spondylolisthesis;
- Presence of bleeding diatheses/coagulation disorder;
- Presence of systemic infection.

Technique

Minimally invasive lumbar decompression is a procedure designed to debulk hypertrophied LF with a goal of relieving neural compression causing symptoms of neurogenic claudication. *mild* selectively removes small portions of ligament and leaves no implants behind. The procedure is performed percutaneously through a 5.1-mm port with specially designed, minimally invasive instruments. Careful review of cross-sectional images of the index level (MRI or CT) allows assessment of the available epidural space, thickness of the LF, potential mechanical impediments to instrument entry and angles of lamina entry (Figure 2).

After a thorough evaluation of imaging, the patient is placed in prone position with a bolster or other positioning aid to reduce lumbar lordosis at the index level. This allows for increased spacing of the lamina and facilitates entry of the working instruments.

The procedure can be done unilaterally or bilaterally, and at multiple symptomatic levels. A working safety barrier is established with either an epidurogram or use of bony landmarks. If using an epidurogram, a baseline preoperative film in all views, including the contralateral oblique view, is obtained (Figure 3). Alternatively, bony landmarks can be used to identify the ventral interlaminar line. The working fluoroscopic angle for the procedure is a contralateral oblique view. The AP image is obtained to ensure that the vertebral bodies of the index level are squared off to best visualize the lamina (Figure 4).

A spinal needle is inserted on the lamina at a pitch commensurate with the sagittal pitch of the index lamina and lateral edge of the spinous process of the inferior lamina, and local anesthesia is used to anesthetize the track

Figure 2. Pitch of lamina determines the working angle (A–C).

Figure 3. Preoperative epidurogram establishes a baseline for evaluating the epidural space and creating a safe visual field to direct the operative devices.

Figure 4. An AP image with the vertebral endplates squared with the fluoroscopic beam is recommended to evaluate the interlaminar space.

Figure 5. *mild* portal stabilizer that mitigates ventral migration of the operating devices while allowing for superior and inferior movement to sculpt the interlaminar space.

Figure 6. Images demonstrating a deployed bone rongeur (A) and tissue sculptor (B) between the lamina and within the epidural space.

and the treatment area. The *mild* trocar/cannula is advanced along the previously made track to rest on the inferior lamina. The contralateral oblique view is again obtained when the *mild* trocar contacts the superior lamina. A *mild* portal stabilizer is placed on the patient, and the portal is locked in this device (Figure 5).

The trocar is then removed, and the depth guide is clicked onto the top of the portal. The bone rongeur is used to remove biopsy-sized fragments of bone for the purpose of widening the interlaminar space to allow further advancement of the *mild* cannula. This usually requires three passes at the superior lamina and three passes at the inferior lamina. Selective removal of small amounts of lamina should be continued until interlaminar access is achieved. The bone rongeur can be rotated in 360 degrees to enhance dissection. Once the tip of the cannula is placed in the middle of the lamina on the contralateral view, the tissue sculptor is used to remove small sections of LF (Figure 6). Approximately three sets of three passes with the tissue sculptor are required for proper debulking.

When there is no longer material to debulk and the instrument ‘falls in the channel’ created by the decompression, the procedure is complete.

The procedure is then performed at the opposite side, and other levels, if appropriate. Following treatment with *mild*, patients typically resume normal activity within 24 h with no restrictions and begin prescribed physical therapy at 2 weeks post procedure.

Discussion

Neurogenic claudication secondary to spinal stenosis is a common condition in the adult population. Although several conservative measures including ESIs have been tried in the past, their efficacy in managing this condition is limited [8]. PILD provides a safe and effective method for the treatment of such patients. It involves decompression of the posterior elements of the spine (lamina and LF) in a minimally invasive fashion and leaves no implants behind. Currently, *mild* is the only commercially available PILD device.

To date, there have been two level 1 RCTs, five prospective studies, two meta-analyses, four retrospective studies, and three case series published demonstrating the safety and efficacy of the *mild* procedure in treatment of LSS secondary to LFH (Table 1). All of these studies have demonstrated efficacy of this procedure in decreasing the symptoms of neurogenic claudication and have shown significant improvements in physical functionality, mobility and disability seen with this condition. Specifically, the ENCORE RCT provided level 1 evidence of the statistical superiority of *mild* versus ESIs in the treatment of patients with neurogenic claudication and LFH at 1-year follow-up [22]. The ENCORE Investigators also reported excellent long-term durability of the *mild* procedure with all outcome measures exhibiting clinically meaningful and statistically significant improvement from baseline through 6-month, 1- and 2-year follow-ups [24]. At 2 years, ENCORE Numeric Pain Rating Scale responders improved by 5 points. Mekhail *et al.* at Cleveland Clinic conducted a study focused on functional outcomes including Standing time and walking distance. At 1 year, walking distance increased 16-fold from 246 feet to 3956 feet, and standing time increased sevenfold from 8 to 56 min [25].

The *mild* clinical studies have adequately demonstrated its effectiveness in treating symptoms secondary to neurogenic claudication – even in patients with multiple types of stenosis and comorbidities. Although it has been reported that LFH contributes up to 85% of central canal narrowing and hypertrophied ligament plays a dominant role in the load-induced narrowing of the lumbar spine [12], other types of stenosis and spinal comorbidities are also common. In the ENCORE study, only 5% of patients presented with central canal stenosis alone, and 95% of patients presented with five or more spinal comorbidities. *mild* has established excellent efficacy in the presence of multiple other comorbidities, as well as lateral and foraminal stenosis. The *mild* procedure removes the problem in the form of hypertrophied ligament and leaves no implants behind. This success is likely related to the fact that although small increments in LFH may cause painful compression of the spinal cord, conversely very small amounts of LF removal can significantly and broadly decrease pain in these patients [25]. This may be analogous to the study published by Choy *et al.* who demonstrated that a small decrease in disc volume can result in large change in intradiscal pressure resulting in relief of discogenic low back pain [42].

These studies have also shown that the *mild* procedure is as safe as an ESI, with minimal complications and durable effect. *mild* offers a minimally invasive solution for a broad range of LSS patients suffering from neurogenic claudication with multiple comorbidities in addition to LFH. Further, in certain patient populations, such as those with severe osteoporosis where an interspinous spacer may be contraindicated and lumbar fusion carries the risk of cage subsidence and pedicle screw loosening [43], the *mild* procedure is an effective and safe alternative. In addition, *mild* may be the only available treatment option for patients with L5-S1 stenosis secondary to LFH who are not candidates for spinal surgery. Almost all clinical studies for *mild* assessed patients for procedure-related complications including dural tears, nerve root injuries, bleeding, infections and rehospitalization post procedure. Direct procedure-related complications were reported to be minimal and included soreness at the surgical site [28], minor postoperative bleeding [27] and minor intraoperative bleeding that was controlled with gel foam [22]. Even though there are no direct comparative safety studies available between *mild* and other decompression procedures (interspinous spacers, surgical decompression and lumbar fusion), pooled data from various studies suggest that *mild* is the safest among these procedures with minimal complications (Table 2) [24].

Although the *mild* procedure is an attractive alternative to other decompression procedures, it is not without its limitations/disadvantages (Table 3). *mild* cannot be performed at the site of previous spine surgery. In addition, it is used to treat spinal stenosis secondary to LFH and does not directly treat stenosis secondary to other etiologies such as disc prolapse or facet hypertrophy, in the absence of LFH. However, presence of other spinal comorbidities

Table 1. Evidence for efficacy.

Study (year)	Study design	Patients (n) & selection criteria	Control	Interventions	Follow-up period	Outcome measures	Results	Conclusion	Ref.
Deer et al. (2010)	Retrospective multicenter observational study	n = 90; Symptomatic L5/S1 failed conservative therapy	–	<i>mild</i> procedure	–	Incidence of dural puncture/tear, blood transfusion, nerve injury, epidural bleeding, hematoma	There were no major adverse events or complications related to the devices or procedure. No incidents of dural puncture or tear, blood transfusion, nerve injury, epidural bleeding or hematoma were observed	The <i>mild</i> procedure is a safe treatment option, and complication rates associated with this procedure may be lower than the complication rates reported for both open and minimally invasive LSS surgeries. However, additional studies with larger patient populations are needed for further evaluation	[26]
Chopko et al. (MIDAS I) (2010)	Prospective, multicenter study	n = 78; Symptomatic L5/S1 failed conservative therapy	–	<i>mild</i> procedure	6 weeks	VAS, ODI, ZCQ, SF-12v2® Health Survey	At 6 weeks, results showed statistically and clinically significant reduction of pain, and improved mobility and physical functionality as measured by VAS, ODI, ZCQ and SF-12v2. Average baseline VAS was 7.3 (3–10); at 6-week follow-up, average VAS improved to 3.7 (0–10), demonstrating a mean improvement of 3.6 from baseline to 6-week follow-up ($p < 0.0001$). For mobility, average baseline ODI was 47.4 (16–84); at 6-week follow-up, average ODI improved to 29.5 (0–72), demonstrating a mean improvement of 17.9 from baseline to 6-week follow-up ($p < 0.0001$). ZCQ physical function and symptom severity (in both pain and neuro-ischemic sub-domains) were statistically significantly improved ($p < 0.001$, paired t-test) from baseline and patients were satisfied with their outcomes. For SF-12v2, health status was improved for the two summary surveys (PCS and MCS) and all eight survey scales at 6-week follow-up compared with baseline. This improvement was statistically significant (95% CI) for all but the GH survey scale. There were no major device or procedure-related complications reported	The <i>mild</i> procedure has good therapeutic efficacy for lumbar spinal canal stenosis, but additional studies are needed for further evaluation	[27]
Linggreen et al. (2010)	Retrospective study	n = 42; Symptomatic L5/S1 failed conservative therapy	–	<i>mild</i> procedure	30 days	VAS	Baseline mean VAS of 9.6 (± 0.42) with standing and ambulation decreased to 5.8 (± 2.5) at 30 days post procedure ($p < 0.05$). All patients reported functional impairment prior to the procedure; 71% reported improvement in function following the <i>mild</i> procedure. There were no major adverse events reported	The <i>mild</i> procedure is a safe and effective treatment modality for neurogenic claudication attributed to central stenosis due to ligamentum flavum hypertrophy in patients who have failed conservative therapy. Further RCTs comparing safety and efficacy of the <i>mild</i> procedure to other treatments for spinal stenosis are warranted	[28]

ESI: Epidural steroid injection; GH: General health; LSS: Lumbar spinal stenosis; MCS: Mental Component Summary; NA: Not applicable; NIH PROMIS: National Institutes of Health Patient-Reported Outcomes Measurement Information System; NPRS: Numeric Pain Rating Scale; NRS: Numerical Rating Scale; ODI: Oswestry Disability Index; PCS: Physical Component Summary; PDI: Pain Disability Index; PRL: Percutaneous remodeling of ligamentum flavum and lamina; QALY: Quality-adjusted life years; RCT: Randomized controlled trial; SF-12v2®: Short Form-12 Version 2 Health Survey; VAS: Visual Analog Scale; ZCQ: Zurich Claudication Questionnaire.

Table 1. Evidence for efficacy (cont.).

Study (year)	Study design	Patients (n) & selection criteria	Control	Interventions	Follow-up period	Outcome measures	Results	Conclusion	Ref.
Chopko (2011)	Case series	n = 14; symptomatic LSS; failed conservative therapy	–	PRL technique (mild procedure)	Average follow-up of 23.5 weeks	VAS, ODI	Mean preoperative VAS was 7.61 ± 2.0 , whereas the average postoperative VAS score was 3.61 ± 2.9 , which demonstrated statistically significant improvement of 52.6% ($p = 0.05$) ODI scores decreased from a preoperative average of 50% to a postoperative average of 43.9%, but the change was not statistically significant No obvious dural tears, CSF leaks or wound-healing complications were observed	The mild procedure is a safe procedure and showed therapeutic efficacy to treat LSS in high-risk patients	[29]
Schomer et al. (2011)	Meta-analysis	n = 107; symptomatic LSS; failed conservative therapy	–	mild procedure	3 months	VAS, ODI	Average baseline VAS of 7.4, decreased to 3.9 at 3-month follow-up, a statistically significant improvement of 3.5 points ($p < 0.0001$) Mean baseline ODI of 48.0 decreased to 30.9 at 3-month follow-up, a statistically significant improvement of 17.1 points ($p < 0.0001$)	When compared with open surgery, mild efficacy results compare favorably, and complication rates are much lower	[30]
Basu et al. (2012)	Case series	n = 27; symptomatic LSS; failed conservative therapy	–	mild procedure	6 months	VAS, ODI, ZCQ	Patients experienced a statistically significant improvement in the VAS pain score from a mean of $9.1 (95\% \text{ CI } \pm 0.59)$ at baseline to $3.9 (95\% \text{ CI } \pm 2.25)$ 6 months after the mild procedure, an improvement of 5.2 points ($p < 0.0001$) Baseline average ODI of $55.1 (95\% \text{ CI } \pm 6.34)$ showed statistically significant improvement at 6-month follow-up with a mean ODI of $31.1 (95\% \text{ CI } \pm 9.29)$, an improvement of 24.0 points ($p < 0.0004$) ZCQ change was statistically significant and demonstrated improvement in all domains ($p < 0.001$). The average ZCQ Patient Satisfaction score was $1.86 (95\% \text{ CI } \pm 0.34)$ at 6-month follow-up, indicating that patients were 'satisfied' to 'very satisfied' with the treatment There were no significant mild device or procedure-related adverse events observed or reported	The mild procedure has been shown to be a safe, effective and cost-effective treatment for LSS patients with neurogenic claudication. However, further randomized, prospective clinical studies would be beneficial	[31]
Deer et al. (2012)	Prospective, single-center study	n = 46; symptomatic LSS; failed conservative treatment	–	mild procedure	12 weeks, 6 months, and 1 year	VAS, ODI, ZCQ	Mean baseline VAS of $6.9 (95\% \text{ CI } \pm 0.6)$ improved to $4.0 (95\% \text{ CI } \pm 1.0)$ at 1-year follow-up, a 2.9-point improvement ($p < 0.0001$) Mean baseline ODI of $49.4 (95\% \text{ CI } \pm 2.5)$ improved to $32.0 (95\% \text{ CI } \pm 5.8)$ at 1-year follow-up, a 17.4-point improvement ($p < 0.0001$) Statistically significant improvements were achieved in all ZCQ domains, including symptom severity, both symptom severity sub-domains (pain and neuro-Ischemia) and physical function (paired t-test; $p < 0.0001$)	The mild procedure demonstrated statistically and clinically significant improvement in physical function, as well as reduction of pain intensity	[32]

ESI: Epidural steroid injection; GH: General health; LSS: Lumbar spinal stenosis; MCS: Mental Component Summary; NA: Not applicable; NIH PROMIS: National Institutes of Health Patient-Reported Outcomes Measurement Information System; NPRS: Numeric Pain Rating Scale; NRS: Numerical Rating Scale; ODI: Oswestry Disability Index; PCS: Physical Component Summary; PDI: Pain Disability Index; PRL: Percutaneous remodeling of ligamentum flavum and lamina; QALY: Quality-adjusted life years; RCT: Randomized controlled trial; SF-12v2®: Short Form-12 Version 2 Health Survey; VAS: Visual Analog Scale; ZCQ: Zurich Claudication Questionnaire.

Table 1. Evidence for efficacy (cont.).

Study (year)	Study design	Patients (n) & selection criteria	Control	Interventions	Follow-up period	Outcome measures	Results	Conclusion	Ref.
Levy et al. (2012)	Systematic safety review and meta-analysis	n = 373; symptomatic LSS, failed conservative treatment	–	<i>mild</i> procedure	1 year	VAS, ODI, Safety data	Mean baseline VAS of 7.4 decreased to 3.5, resulting in a mean pain improvement of 3.9 (95% CI ± 0.42) at 1-year follow-up. Mean baseline ODI of 46.6 improved to 30.6, a 16.0 point mean mobility improvement at 1-year follow-up There were no reports of major device- or procedure-related adverse events, and there were no mortalities in this study	The <i>mild</i> procedure provides statistically significant improvement in pain and mobility, as well as an excellent safety profile	[33]
Mekhaail et al. (2012)	Prospective single-center study	n = 40; symptomatic LSS, failed conservative treatment	–	<i>mild</i> procedure	1 year	PDI, RMQ, Standing Time, Walking Distance, VAS	Mean baseline PDI of 41.4 decreased to an average of 18.8 at 1 year post procedure, a statistically significant improvement of 55% The mean RMQ baseline score of 14.3 decreased to an average score of 6.6 at 1 year post procedure, a statistically significant improvement of 54% standing time improved from a baseline of 8 to 56 min at 1-year follow-up walking distance improved from a baseline mean of 246 feet to 3956 feet at 1-year follow-up VAS improved from 7.1 at baseline to 3.6 at 1-year follow-up	The <i>mild</i> procedure provides therapeutic efficacy with regard to improved functionality and decreased disability in patients with neurogenic claudication	[25]
Mekhaail et al. (2012)	Prospective, multicenter study	n = 58; symptomatic LSS, failed conservative treatment	–	<i>mild</i> procedure	1 year	VAS, ODI, ZCQ, SF-12v2	Baseline mean VAS of 7.4 (95% CI ± 0.5) improved to a mean of 4.5 (95% CI ± 0.8) at 1-year follow-up, a statistically significant improvement of 2.9 points (p < 0.0001) Baseline average ODI of 48.6 (95% CI ± 3.8) decreased to an average of 36.7 (95% CI ± 5.8) at 1-year follow-up, a statistically significant improvement of 11.9 points (p < 0.0001) Regarding ZCQ, patients in the <i>mild</i> treatment group reported statistically significant improvements in all domains at 1-year follow-up. Average patient satisfaction score was 2.20 (95% CI ± 0.26), and 74% of patients reported that they were satisfied with the outcome of the procedure There were no reports of major intra- or postoperative <i>mild</i> device or procedure-related adverse events	The <i>mild</i> procedure provides therapeutic efficacy and has an excellent safety profile	[34]
Wong (2012)	Case series	n = 17; symptomatic LSS, failed conservative therapy	–	<i>mild</i> procedure	1 year	VAS, ODI	Baseline mean VAS of 7.6 decreased to 2.3 at 1-year follow-up, an improvement of 5.4 (95% CI) Average baseline ODI of 48.4 decreased to 21.7 at 1 year, an improvement of 26.6 points (95% CI) There were no major device- or procedure-related complications	The <i>mild</i> procedure provides significant pain relief and increased mobility for patients with LSS who have failed injection therapy	[35]

ESI: Epidural steroid injection; GH: General health; LSS: Lumbar spinal stenosis; MCS: Mental Component Summary; NA: Not applicable; NIH PROMIS: National Institutes of Health Patient-Reported Outcomes Measurement Information System; NPRS: Numeric Pain Rating Scale; ODI: Oswestry Disability Index; PCS: Physical Component Summary; PDI: Pain Disability Index; PRLI: Percutaneous remodeling of ligamentum flavum and lamina; QALY: Quality-adjusted life years; RCT: Randomized controlled trial; SF-12v2®: Short Form-12 Version 2 Health Survey; VAS: Visual Analog Scale; ZCQ: Zurich Claudication Questionnaire.

Table 1. Evidence for efficacy (cont.).

Study (year)	Study design	Patients (n) & selection criteria	Control	Interventions	Follow-up period	Outcome measures	Results	Conclusion	Ref.
Brown (2012)	Prospective, single-center, double-blind, randomized controlled trial	n = 38; symptomatic L5/S1 failed conservative therapy	ESI	<i>mild</i> procedure	6 and 12 weeks	VAS, ODI, ZCQ	In the <i>mild</i> treatment group, average VAS baseline of 6.3 (95% CI $\pm$ 0.7) improved to a mean of 3.8 (95% CI $\pm$ 1.3) at 6-week follow-up and to a mean of 3.4 at 12-week follow-up (the change from baseline to week 6 and baseline to week 12 was significant ($p < 0.01$), but the change from 6 weeks to 12 weeks was not significant). In the ESI treatment group, mean VAS was 6.4 (95% CI $\pm$ 1.0) at baseline compared with 6.3 (95% CI $\pm$ 1.4) at 6-week follow-up, an insignificant improvement of 0.1 points, which was not statistically significant ($p > 0.05$). In the <i>mild</i> treatment group, mean ODI at baseline was 38.8 (95% CI $\pm$ 4.2) compared with a mean of 27.4 (95% CI $\pm$ 7.0) at 6-week follow-up, an improvement of 11.4 points. At 12 weeks, ODI improved by a mean of 18.6 in the <i>mild</i> treatment group. The change from baseline to 6 weeks post <i>mild</i> and baseline to 12 weeks post <i>mild</i> was significant ($p < 0.05$ and $p < 0.01$, respectively), but the change from 6 weeks to 12 weeks was not significant ($p > 0.05$). In the ESI treatment group, the mean baseline ODI was 40.5 (95% CI $\pm$ 5.9) and improved to 34.8 (95% CI $\pm$ 8.2) at 6-week follow-up, an improvement of 5.7 points, which was not statistically significant ($p > 0.05$). At 6-week follow-up, the mean ZCQ Patient Satisfaction score for the <i>mild</i> treatment group was 2.2 (95% CI $\pm$ 0.5) and 2.8 (95% CI $\pm$ 0.5) for the ESI treatment group. At 12-week follow-up, the average ZCQ patient satisfaction score was 1.8 for <i>mild</i> indicating a high level of patient satisfaction. No major <i>mild</i> or ESI device or procedure-related complications were reported	The <i>mild</i> procedure provides statistically significantly better pain reduction and improved functional mobility compared with treatment with ESI	[36]
ESI: Epidural steroid injection; GH: General health; LSS: Lumbar spinal stenosis; MCS: Mental Component Summary; NA: Not applicable; NIH PROMIS: National Institutes of Health Patient-Reported Outcomes Measurement Information System; NPRS: Numeric Pain Rating Scale; ODI: Oswestry Disability Index; PCS: Physical Component Summary; PDI: Pain Disability Index; PRL: Percutaneous remodeling of ligamentum flavum and lamina; QALY: Quality-adjusted life years; RCT: Randomized controlled trial; SF-12v2®: Short Form-12 Version 2 Health Survey; VAS: Visual Analog Scale; ZCQ: Zurich Claudication Questionnaire.									

Table 1. Evidence for efficacy (cont.).

Study (year)	Study design	Patients (n) & selection criteria	Control	Interventions	Follow-up period	Outcome measures	Results	Conclusion	Ref.
Durkin et al. (2013)	Retrospective observational study	n = 50; symptomatic LSS; failed conservative therapy	–	<i>mild</i> procedure	1, 3 and 6 months	NRS, ZCQ, ODI, NIH PROMIS, patients' self-reported low back and lower extremity pain distribution	Mean baseline NRS of 7.52 (4–10) improved to an average of 5.18 (0–10) at 1 month, 5.31 (0–10) at 3 months and 5.60 (0–10) at 6-month follow-up ($p < 0.0001$) Mean baseline ODI of 40.58 (10–78) improved to an average of 32.52 (0–62.22) at 1 month ($p = 0.0002$), 32.22 (0–66) at 3 months ($p = 0.0002$) and 29.24 (0–73.33) at 6-month follow-up ($p = 0.0004$) Mean baseline NIH PROMIS score of 63.39 improved to an average of 58.53 at 1 month ($p = 0.0006$), 58.88 at 3 months ($p = 0.008$) and 58.30 at 6-month follow-up ($p = 0.014$) For patients' self-reported pain patterns, 64.3% of <i>mild</i> patients at 3 months reported that their pain was less; 35.7% of patients also reported no pain at 3 months post procedure. However, 19% of <i>mild</i> patients at 3 months did not indicate reduction in leg pain when standing and walking; 16.7% of patients reported worsening of their pain compared with baseline For ZCQ, 31.7% of <i>mild</i> patients at 3 months and 22% of <i>mild</i> patients at 6 months experienced a 'clinically meaningful' ZCQ pain score reduction of at least 20% post <i>mild</i>	The <i>mild</i> procedure holds great promise to improve pain and functional outcomes for LSS patients. Further studies are warranted	[37]
Chopko (2013)	Prospective, multicenter study	n = 45; symptomatic LSS; failed conservative therapy	–	<i>mild</i> procedure	2 years	VAS, ODI, ZCQ	Mean baseline VAS of 7.2 (95% CI ± 0.6) decreased to 4.8 (95% CI ± 0.8) at 2-year follow-up, a statistically significant improvement of 2.4 points ($p < 0.0001$) Average baseline ODI of 48.4 (95% CI ± 4.4) decreased to 39.8 (95% CI ± 5.6) at 2-year follow-up, a statistically significant improvement of 8.6 points ($p < 0.0001$) All ZCQ domains showed statistically significant improvement at 2-year follow-up, including the physical function domain ($p = 0.0006$), and both the pain subdomain ($p < 0.0001$) and the neuroischemic subdomain ($p = 0.0002$). No major device or intraprocedural adverse events were reported.	The <i>mild</i> procedure provides therapeutic efficacy for patients with neurogenic claudication associated with LSS	[38]
Wang et al. (2013)	Health economics	n = 22; symptomatic LSS; failed conservative therapy	–	<i>mild</i> procedure	–	The amount of time spent in specialty care and the number of interventional procedures performed before and after <i>mild</i>	The mean chronic pain management resource usage was 9.33 between initial consultation and receiving <i>mild</i> and improved to 5.11 post <i>mild</i> . Prior to undergoing the <i>mild</i> procedure, these patients received an average of 0.395 interventional pain procedures per month	Not only is <i>mild</i> a reliable method to treat LSS, but <i>mild</i> also appears to reduce the consumption of limited healthcare resources	[39]

ESI: Epidural steroid injection; GH: General health; LSS: Lumbar spinal stenosis; MCS: Mental Component Summary; NA: Not applicable; NIH PROMIS: National Institutes of Health Patient-Reported Outcomes Measurement Information System; NPRS: Numeric Pain Rating Scale; NRS: Numerical Rating Scale; ODI: Oswestry Disability Index; PCS: Physical Component Summary; PDI: Pain Disability Index; PRL: Percutaneous remodeling of ligamentum flavum and lamina; QALY: Quality-adjusted life years; RCT: Randomized controlled trial; SF-12v2®: Short Form-12 Version 2 Health Survey; VAS: Visual Analog Scale; ZCQ: Zurich Claudication Questionnaire.

Table 1. Evidence for efficacy (cont.).

Study (year)	Study design	Patients (n) & selection criteria	Control	Interventions	Follow-up period	Outcome measures	Results	Conclusion	Ref.
Udeh et al. (2015)	Cost-effectiveness analysis using decision analytic model	NA	ESI, laminectomy	<i>mild</i> procedure	2 years	QALY	The optimal choice in terms of costs and benefits was the <i>mild</i> strategy at \$43,760 per QALY. The next best alternative was ESI at an additional \$37,758 per QALY. Laminectomy surgery demonstrated to be both more costly and less effective than either <i>mild</i> or ESI according to the baseline analysis (\$125,985 per QALY)	The <i>mild</i> procedure is a cost-effective alternative for appropriate patients rather than continuing with conservative treatment and repeated serial ESI or proceeding to laminectomy surgery	[40]
Benjamin et al. (2016)	Prospective, multicenter, randomized controlled trial	n = 302; symptomatic LSS; failed conservative therapy	ESI	<i>mild</i> procedure	6 months, 1 year	ODI, NPRS, ZCQ	At 1-year follow-up, ODI, NPRS and all ZCQ domains demonstrated statistically significant superiority of <i>mild</i> vs ESIs. For primary efficacy, the ODI responder rate in the <i>mild</i> group was statistically significantly higher than the responder rate in the ESI group ($p < 0.001$). Within-group change in the <i>mild</i> group from baseline to 1-year follow-up for all efficacy end points including ODI, NPRS, ZCQ physical function and ZCQ symptom severity was statistically significant ($p < 0.001$). The ZCQ Patient Satisfaction score for <i>mild</i> demonstrated a statistically significantly higher level of patient satisfaction with the <i>mild</i> procedure vs ESIs. There were no significant differences in the safety profiles between groups	This RCT provides level I evidence of the superior effectiveness of <i>mild</i> vs ESIs in the treatment of LSS patients with neurogenic claudication associated with central stenosis due to ligamentum flavum hypertrophy	[22]
Staats et al. (2018)	Prospective, multicenter, randomized controlled trial	n = 143; symptomatic LSS; failed conservative therapy	–	<i>mild</i> procedure	6 months, 1 year, 2 years	ODI, NPRS, ZCQ	At 2 years, ODI improved by 22.7 points (95% CI, 18.5–26.9), NPRS improved by 3.6 points (95% CI, 3.1–4.2), and ZCQ symptom severity and physical function domains improved by 1.0 (95% CI, 0.8–1.2) and 0.8 points (95% CI, 0.6–0.9), respectively. During 2-year follow-up, 8 of 143 (5.6%) patients underwent a subsequent surgical procedure at the index level, 22 of 143 received an ESI or nerve block at the level of surgery, and one of these patients also received a spinal cord stimulator as a treatment for the pain at the index level. One additional patient received a rhizotomy at the index level, and one patient received an intrathecal infusion pump. There were no serious device/procedure-related adverse events, and 1.3% experienced a device-or procedure-related adverse event	The <i>mild</i> procedure provides therapeutic efficacy and is an excellent choice for first-line therapy for select patients with central spinal stenosis suffering from neurogenic claudication symptoms with hypertrophic ligamentum flavum	[24]
Jassal (2019)	Retrospective single-center study	n = 20, symptomatic LSS; failed conservative therapy	–	<i>mild</i> procedure	6 months	VAS, Opioid reduction	Of the 20 patients evaluated at 6-month follow-up post <i>mild</i> , there was a 64% reduction in opioid use and a 72% improvement in VAS scores	The <i>mild</i> procedure demonstrated significant pain relief, and reduction of opioids and improvement in VAS score	[41]

ESI: Epidural steroid injection; GH: General health; LSS: Lumbar spinal stenosis; MCS: Mental Component Summary; NA: Not applicable; NIH PROMIS: National Institutes of Health Patient-Reported Outcomes Measurement Information System; NPRS: Numeric Pain Rating Scale; ODI: Oswestry Disability Index; PCS: Physical Component Summary; PDI: Pain Disability Index; PRLL: Percutaneous remodeling of ligamentum flavum and lamina; QALY: Quality-adjusted life years; RCT: Randomized controlled trial; SF-12v2®: Short Form-12 Version 2 Health Survey; VAS: Visual Analog Scale; ZCQ: Zurich Claudication Questionnaire.

Table 2. Comparison of complications between various decompression procedures.

2-year outcomes	mild [†]	Interspinous process distraction		Surgical decompression [‡]	Fusion [§]
		Superion [¶]	X-Stop [#]		
Reoperation	5.6%	20%	14.4–26%	6–7.8%	12.5–16.9%
Device- and procedure-related adverse events	1.3%	Device		Intraoperative: 9.9%	23.3%
		11.6%	7.5%		
		Procedure related			
		14.2%	15.9%		
Device and procedure-related serious AEs	0%	8.4%	9.5%	Postoperative: 12.3%	6% late
Lumbar spine fractures	0%	16.3%	8.5%	–	4.2%
Removal of hardware	No implants	16.3%	12.4%	No implants	4.3%

mild (Vertos Medical, CA, USA), Superion (Vertiflex, CA, USA), X-Stop (Medtronic, CA, USA).

[†]Data taken from [24].

[‡]Data taken from [44,45].

[§]Data taken from [46–50].

[¶]Data taken from [51].

[#]Data taken from [44,51].

Created using data from [24].

Table 3. Comparing advantages and disadvantages of the *mild* procedure.

Advantages	Disadvantages & limitations
- Broad patient selection: neurogenic claudication + ligamentum flavum hypertrophy (≥ 2.5 mm) – even in patients with comorbidities - As safe as an epidural steroid injection - Lowest complication rate vs other lumbar spinal stenosis treatments - Low reoperation rates - Clinically significant long-term improvement in mobility and reduction in pain - Minimally invasive procedure - Intact spinal anatomy and minimal tissue trauma - No implants - Steroid-free procedure, thereby limiting immunosuppression risk - No requirement for general anesthesia or hospital stay - Resumption of normal activity within 24 h with no restrictions - Maintenance of range of motion – both flexion and extension - No contraindication for patients with osteoporosis - No limitations regarding future interventions - Cost effective	- Treatment of stenosis secondary to ligamentum flavum hypertrophy - Contraindication for performing at site of previous surgery - Some radiation exposure

does not disqualify a patient as a candidate for undergoing the *mild* procedure. The minimally invasive spine treatment guidelines recommend use of PILD as the first-line therapy for treatment of LSS if there is presence of LFH ≥ 2.5 mm and absence of any contraindications, irrespective of presence/absence of other comorbidities that may contribute to spinal stenosis [9].

Future perspective

With safety and efficacy of the *mild* procedure well established, there has been positive growth with coverage by a national payer and self-insureds. At present, all medicare administrative contractors cover the *mild* procedure, an insurer that covers the age group most likely applicable for the procedure. Large self-insured plans such as Walmart's Centers of Excellence program also cover *mild*. Although head-to-head trials between *mild* and invasive surgical techniques are not permissible because the patient populations are not identical, it is important that clinical studies are conducted to build on the existing body of evidence supporting the use of this procedure versus conventional medical management. One such ongoing study is the MOTION Study (NCT03610737), which is a multicenter RCT comparing the *mild* procedure together with conventional medical management to conventional medical management alone in the treatment of LSS in a cohort of 150 patients [52]. The primary outcome measure of the study is the Oswestry Disability Index, along with secondary outcome measures including the Numeric Pain Rating Scale, the Zurich Claudication Questionnaire, walking distance, and walking time to symptoms. Main inclusion criteria of the study are LSS with neurogenic claudication with evidence of LFH ≥ 2.5 mm on imaging. Main exclusion criteria of the study are an Oswestry Disability Index Score < 31 , Numeric Pain Rating Scale < 5 and prior surgery/interspinous spacer/*mild* procedure/vertebral augmentation/intradiscal procedure at

the same treatment level. The estimated completion of the study is early 2022. Another ongoing study is the *mild*® Percutaneous Image-Guided Lumbar Decompression: A Medicare Claims Study (NCT03072927) [53]. This is a prospective longitudinal study comparing outcomes of Medicare beneficiaries treated with *mild* versus those treated with interspinous process decompression at the 24-month follow-up. Primary outcome measures will include the rate of surgery or minimally invasive intervention in the patient post index procedure and the rate of participants with harms associated with the index procedure.

Conclusion

mild is a minimally invasive spine procedure for the treatment of LSS secondary to LFH that does not involve the use of implants. When used judiciously, *mild* has demonstrated excellent efficacy and safety in 13 peer-reviewed studies. Although treatment plans for these patients usually begin with a regimen of conservative care, subsequent treatment decisions generally favor the least invasive and safest options that may provide relief. With an established safety profile equivalent to ESIs, and efficacy that has been shown to be superior to ESIs, *mild* can reasonably be positioned early in the treatment algorithm for these patients. Based on extensive review of the literature, robust safety and efficacy through 2 years, and in line with the minimally invasive spine treatment guidelines, we recommend that *mild* be considered as the first intervention after failure of conservative measures for patients diagnosed with LSS and LFH ≥ 2.5 mm showing signs/symptoms of neurogenic claudication.

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