REVIEW

Lumbar Spinal Stenosis and Minimally Invasive Lumbar Decompression: A Narrative Review

Hongjie Yuan[1], Xiaobin Yi[2]

[1]Department of Pain Medicine, Xinhua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, Shanghai, People's Republic of China; [2]Pain Division, Department of Anesthesiology, Washington University in St Louis, St Louis, MO, USA

Correspondence: Xiaobin Yi, Email yix@wustl.edu

Background: Lumbar spinal stenosis (LSS) is a common pain condition that causes lumbar back pain, radiating leg pain, and possible functional impairment. *MILD* is an emerging minimally invasive treatment for LSS. It is an image-guided percutaneous procedure designed to debulk hypertrophied ligamentum flavum. However, the exact short- and long-term efficacy, safety profile, indication criteria, and certain procedure details reported in medical literature vary.

Objective: This narrative review was to elucidate efficacy, safety profile, certain procedure details, advantages, and limitations of *MILD*.

Study Design: This is a narrative review.

Setting: All included articles are clinic trials including analytic studies and descriptive studies.

Methods: PubMed, Cochrane Library, and Scopus were searched. Only clinical trials of *MILD* procedure were included. Information of indications, contraindications, VAS scores, ODI scores, effective rate, efficacy durations, and certain procedure details was focused on.

Results: According to the literature, for the *MILD* procedure, the VAS score could be reduced from a pre-treatment level of 6.3–9.6 to a post-treatment level of 2.3–5.8. The ODI score could be reduced from a pre-treatment level of 38.8–55.3 to a post-treatment level of 27.4–39.8. The effective rate of the *MILD* procedure was reported to be 57.1%–88%. A 2-year postoperative stability of efficacy was also supported. One RCT study testified superior efficacy of *MILD* over epidural steroid injection.

Limitations: There is few high-quality literature in the review. Moreover, the long-term efficacy of *MILD* cannot be revealed according to the current literature.

Conclusion: Based on the reviewed literature, *MILD* is an effective and safe procedure. *MILD* can reduce pain intensity and improve functional status significantly. Therefore, it is a preferable option for LSS patients who failed conservative treatments, but not for those who require immediate invasive decompression surgery.

Keywords: lumbar spinal stenosis, minimally invasive lumbar decompression, *mild* ®, low back pain, lumbar radiculopathy, neurogenic claudication, ligamentum flavum

Introduction

Lumbar spinal stenosis (LSS) is a common pain disorder. The prevalence of symptomatic LSS in adults was reported to be approximately 11% and increased with age.[1] As a common pain disorder, the symptom of LSS is frustrating. The patients usually experience persistent lumbar back pain, lower extremity pain, and possibly lower leg numbness, tingling, and paresthesia. Apart from pain perception or discomfort, the patient's ability to walk is impaired. Typically, the patients cannot walk continuously and require intermittent resting while walking, which is termed neurogenic claudication.[2]

As a common and frustrating disease, the treatment of LSS is complicated and, in some cases, challenging. In most cases, conservative treatments, such as oral medication, physical therapy, and epidural steroid injection, should be chosen first.[3] However, conservative treatments have been reported to have limitations.[4] For example, physical therapy and oral medications do not have a long-lasting effect on LSS.[5] Epidural steroid injection (ESI) has been reported to be ineffective for LSS patients with neurogenic claudication.[6] For those refractory to conservative treatments, surgeries are required. Although invasive surgery is effective, however, its invasiveness and relatively high rate of complications are

3707

disadvantages.[7–9] For those patients who have failed conservative treatment but have contraindications for invasive surgery, or who are unwilling, or not severe enough to advance to more invasive surgical procedures, both physicians and patients are often left with a treatment dilemma. Under these circumstances, minimally invasive procedures are a preferable choice.

Minimally invasive lumbar decompression (*MILD*, Vertos Medical, Aliso Viejo, CA, USA) is an emerging minimal invasive procedure for LSS. It is reported to be a treatment modality with considerable minimal invasiveness, safety, and a high effective rate [10–13]. However, the exact short- and long-term efficacy, safety profile, indication criteria, and certain procedure details reported in medical literature vary. Furthermore, there is a concern about the *MILD* procedure. For *MILD*, as the ligamentum flavum (LF) was not removed wholly, whether the nerve tissue can be decompressed adequately? Is long-term efficacy guaranteed? Therefore, in this review, we elucidate the exact effectiveness, safety profile, and treatment rationale of the *MILD* procedure as well as the pathogenesis and diagnosis of LSS.

Pathogenesis of Lumbar Spinal Stenosis

LSS can be classified into primary stenosis and secondary stenosis. For primary stenosis, the main etiology is congenital abnormalities, which are relatively rare. The secondary etiology contains numerous origins, among which age-related spinal degeneration is the leading origin.[10] In this review, we mainly focus on degenerative LSS.

LSS was defined 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.[11]

Under normal physiological conditions, the vertebral canal has enough reserve space for the spine and nerve roots. On the epidural spaces, fat tissue and epidural veins serve as cushioning pockets for nerve tissues. Therefore, the nerve tissue will not be compressed under physiological conditions. However, along with the aging process, the lumbar spine degenerated. The degenerative changes of the spine may lead to a diminished spinal canal and intervertebral foramen. The central spinal canal, lateral recess canals, and intervertebral foramina are the three main possible anatomic spots to be narrowed.[10] With reserve space in the spinal canal, mild spinal deterioration would not exert nerve tissue compression. However, when spinal degenerative changes deteriorate to a certain extent, nervous structures tend to be compressed, and symptomatic LSS emerges.

Dynamic Components of LSS

Stenosis of the lumbar spine is considered to have both structural background components and dynamic components. In addition to background structural stenosis, lumbar extension or walking can cause further narrowing of the spinal canals, which were regarded as the dynamic components. The transverse area of the L3/4 level was reported to decrease by approximately 40 mm^2 or 16% of reduction when the spine position was shifted from a flexion position with axial pressure to an ab extension position with axial distraction.[12] In vivo study with a spinal myelogram revealed that the cross-sectional area and sagittal diameter were dramatically reduced during lumbar extension and increased during lumbar forward flexion.[13]

Regarding the mechanism of the dynamic component of LSS, several articles have reported that posture-induced or axial pressure-induced elastic deformation of LF was the main contributor.[14–21] Lumbar extension or standing position may cause two adjacent laminas to move closer, followed by LF thickening and infolding. By contrast, lumbar flexion or lying flat position may cause the two-adjacent lamina to separate, resulting in the stretching and thinning of LF as well as the disappearance of LF infolding. There are some quantitative studies. A 12-participant observational study was conducted by Marius R Schmid. The average thickness of the LF during lumbar flexion, as measured by MRI, was 1.8 mm and increased to 4.3 mm during lumbar extension.[15]

Furthermore, the dynamic change in disc bulging degree contributes to the dynamic components of LSS. Under coaxial load, intervertebral disc bulging can be more severe. However, no article has demonstrated that lumbar disc elastic deformation plays a significant role in the dynamic components of LSS. Compared with dynamic changes in LF

thickness, dynamic changes in the degree of disc bulging are not as evident.[14,18] Disc bulging usually acts as a background contributor to LSS.

The following may be the reason. The lumbar disc is a load-bearing structure that possesses a high degree of rigidity. Furthermore, as with most LSS patients, the disc hardened or even calcified because of disc degeneration. Therefore, the disc deformation is minor.

The size and volume of the intervertebral foramina (root canals) increase and decrease dramatically in lumbar flexion (lying flat) and lumbar extension (standing).[16,17] This constitutes the underground mechanism for intervertebral foraminal type LSS.

Nerve Tissue Compression, Blood Ischemia, and Venous Congestion

Because of anatomic spinal canal narrowing, nerve roots, the cauda equina, and epidural vascular tissues can be compressed.[10] For nerve root compression, the nerve fiber proper and nutrient vessels can be compressed, leading to a neuropathic pain condition. In this process, complicated pathologic changes will happen, including ischemia inflammation, disturbance of axoplasmic transport, Wallerian degeneration, and spontaneous action potential bursting.[22,23]

However, for cauda equina compression, the pathology is more complicated as cauda equina are located in the subarachnoid space and suspended in the cerebrospinal fluid. Both cauda equina ischemia, venous congestion, and disturbed cerebrospinal fluid induced by upright exercise can be the etiology.[24,25] Compared with arterial ischemia, venous congestion may be a more significant factor precipitating circulatory disturbance in compressed cauda equina.[26] As a chronic compression, the intra-spinal pressure is usually lower than the arterial pressure, so the arterial blood supply is hardly affected. However, intra-spinal pressure fluctuates. Under the lumbar extension position, intra-spinal pressure would increase to a level higher than venous pressure, the venous return was blocked, and venous congestion would happen. Whereas under the lumbar flexion position, the intra-spinal pressure would decrease to a level below venous pressure, the venous return would recover, and venous congestion would relieve gradually.[25] This pathological condition is more obvious in multiple-level stenosis.[25] Increased mechanical compression in the cauda equina also disrupts the CSF flow. Venous hypertension and disturbance in the CSF flow are inducing factors for blood-nerve barrier damage. Therefore, intra-radicular edema and ischemia of cauda equina would occur, resulting in neurogenic claudication.[27]

Clinical Manifestations of LSS

The clinical manifestations of LSS are heterogeneous.

Lumbar Back Pain and Radiculopathy

Patients with LSS may experience lumbar back pain and radiating pain to unilateral or bilateral buttocks, and a certain part of the legs. The pain usually has an insidious onset and persists for a long time with an intermittent remission period. Some patients may experience bilateral or unilateral leg numbness, tingling, weakness, and cooling. The patients may also exhibit leg weakness and poor walking balance.

Neurogenic Claudication

The characteristic symptom of LSS is exercise- or position-induced neurogenic claudication, which means that lumbar extension or upright walking may cause onset or aggravation of symptoms, whereas lumbar flexion spine or sitting may cause symptoms to disappear or relief.[10] The patients were unable to walk continuously and must sit for a while before continuing to walk.

Cauda Equina Syndrome

In some serious cases, LSS patients may have cauda equina syndrome. Diverse symptoms characterize cauda equina syndrome. The patients may have a certain level of lower leg weakness. The weakness may be unilateral or bilateral, involving more than one nerve segment. Bowel and bladder dysfunction, involving urinary incontinence or retention, may also be accompanied by fecal incontinence. Saddle anesthesia and sexual functional dysfunction are also common symptoms of cauda equina syndrome.

Physical Examination

In LSS patients, motor, sensory and reflex testing may be normal but may be diminished in severe cases. In contrast to lumbar disc herniation, the majority of patients fail the straight leg raising test. Multiple tender points in the lumbar region may exist. It is possible to detect paresthesia or hypoesthesia in the distribution of the affected nerve root or the saddle area.

Image Studies

MRI

MRI is regarded as the standard imaging modality for LSS.[28] It shows the spinal cord, dural sac, nerve roots, and surrounding areas, such as the lumbar disc, LF, fat tissues, and blood vessels around the nerves. In MRI, the nerves and dural sac compression can be clearly outlined.

CT and CT Myelography

CT and CT myelography reveals the bony structures of the spine, such as vertebrae, vertebral arch, the spinal canal, and the intervertebral disc. It is possible to clearly illustrate disc bulging, protrusion or hypertrophy, facet joint hypertrophy, or calcification. The spinal canal and intervertebral foramen stenosis could also be illustrated. As CT myelography can outline the dural sac, CT myelography may be an alternative option for patients who cannot undergo MRI.[11,28]

MRI or CT with Axial Loading

MRI or CT with axial loading is recommended for participants with typical symptoms that cannot be confirmed with a standard MRI or CT.

X-Ray

X-ray reveals the bone structure, lumbar curvature, and joint outline. X-rays can demonstrate the diagnosis of spondylolisthesis. Flexion-extension position film is warranted to rule out lumbar instability.

Lower Extremity Vascular Ultrasonography and Angiography

These are recommended to rule out vasogenic intermittent claudication in certain circumstances.

Diagnostic Criteria of Image Studies

As the diagnosis of LSS should be based on multiple factors, the reported quantitative criteria varied.[3,29–31] The quantitative criteria of image study are far more from a gold diagnostic standard and can only provide a reference value for the diagnosis of LSS.

For Central Canal Stenosis

Median sagittal diameter of osseous spinal canal < 7–13 mm and/or cross-sectional area of dural sac < 100 mm^2 was regarded as central canal stenosis.

For Lateral Recess Stenosis

Lateral recess height (the anterior point of the superior articular surface to the posterior border of vertebrae) < 2 mm and the lateral recess angle < 30° were all indicators for lateral recess stenosis.

For Foraminal Stenosis

Foraminal height < 3 mm was regarded as foraminal stenosis. However, some articles have suggested that the disappearance of the fat tissue surrounding the nerve roots is a more accurate indicator.[32]

Laboratory Test

Laboratory screening tests consisting of a complete blood count, erythrocyte sedimentation rate, antinuclear antibody testing, HLA-B27 antigen screening, and automated blood chemistry testing are usually within normal limits. These tests can help rule out other potential causes of the patient's pain.

Diagnosis

The clinical diagnosis of spinal stenosis is supported by a combination of clinical history, clinical manifestation, physical examination, and imaging study results.[10] Furthermore, differential diagnosis is essential. For example, detailed acquisition of medical history and clinical manifestation, as well as additional tests to rule out other confounding conditions including vascular claudication, are essential.

Paradigm of Treatment

Lumbar decompression such as laminectomy with or without lumbar fusion is required for patients with cauda equina syndrome or severe progressive neurologic function impairment, such as true motor weakness. For LSS patients without the aforementioned conditions, the treatment options should be applied ladder-like. Conservative measures include activity modification, non-steroidal anti-inflammatory drugs, oral analgesics, braces for instability, physical therapy, and epidural steroid injections; these treatments should be applied initially.[1] We considered these conservative treatments to be the initial ladder treatments. For patients who have failed conservative therapies and are not surgical candidates because of co-morbid conditions, minimal invasive treatments are advisable options. Minimally invasive treatments include the *MILD* procedure and the implantation of a percutaneous interspinous spacer. We regard minimally invasive treatments to be the second ladder. Invasive surgery, such as laminectomy with or without vertebral fusion, is considered to be the third step therapeutic option for patients who have failed three to six months of conservative treatment or minimally invasive treatments.

Minimally Invasive Lumbar Decompression

History of *MILD*

The first *MILD* instrument was invented in 2005 by Dr. David Solsberg and Dr. Donald Schomer. It was first designed to treat LSS patients with malignant comorbidities who were unable to tolerate open surgery. It was named X-Sten *MILD* Tool Kit and received FDA approval in December, 2006. Since then, multiple hospitals have implemented the *MILD* procedure and clinical trials about *MILD*. In 2016, Benyamin et al implemented a level 1 RCT trial. The trial demonstrated superior efficacy of *MILD* over ESI at 1-year follow-up. Based on this level 1 evidence, the *MILD* procedure was approved coverage nationwide by the US Centers for Medicare and Medicaid Services in 2017.[33]

Indications and Contraindications of *MILD*

Indications

1. LSS patients with neurogenic claudication.
2. Symptoms (see below) persist for more than 3 months.
3. Failed conservative treatments.
4. Radiologic evidence:
   (a) LF thickness > 2.5 mm,
   (b) central canal cross-sectional area □ 100 mm^2

Symptoms of LSS Include

1. Pain is located in the lumbar back, unilateral or bilateral buttocks, and legs.
2. The pain can be aggravated while upright walking or standing, and relieved when bending forward or sitting down.
3. Lean forward during walking.
4. Unable to stand upright and unaided for more than 15 minutes.
5. Unable to walk unaided in an upright position for more than one-quarter mile.

Contraindication

1. History of prior surgery at the same treatment level.
2. Lumbar spondylolisthesis > Grade 1.
3. Significant symptomatic disc protrusion
4. Excessive facet hypertrophy or osteophyte formation
5. Symptomatic lateral recess stenosis.
6. Inability to walk ≥ 10 feet unaided.
7. Symptomatic epidural lipomatosis
8. Bleeding disorders.
9. Under anticoagulation therapy.
10. Wound healing disorders, such as diabetes and malignant disease
11. Inability to keep a prone position even under anesthesia.
12. Inability to sign informed consents

Disagreement About Lumbar Spondylolisthesis as a contraindication

The MiDAS Encore study suggests that lumbar spondylolisthesis with Grade ≤ 2 was the indication, whereas all of the other articles insisted that only Lumbar spondylolisthesis with Grade ≤ 1 was the indication.[33]

Disagreements About Lateral Recess Stenosis

The MiDAS Encore study clearly outlines that only central stenosis was eligible for *MILD*; however, this criterion was not mentioned in any other article. Therefore, additional research is necessitated to evaluate whether *MILD* is an eligible treatment for LSS of lateral recess stenosis.

Disagreements About the Thickness of LF

In Mekhail's study, the thickness of LF > 4mm was regarded as an indication.[34] However, the thickness of LF > 2.5 mm has been commonly cited as an indication in the remaining articles.[35–39] Some articles have not regarded the thickness of LF as an indication factor.[40–42]

Surgery Details of *MILD*

Before the surgery, a CT or MRI is reviewed to identify the responsible level, as well as to observe the inter-laminar space windows and the stenosis degree, which is the thickness of the LF. The details of operation please refer to the previous literature.[41]

Is Epidurogram Necessary?

In most reports, epidurogram was recommended. Epidurogram aimed to identify the border between the dural and epidural space before and during the procedure. It was supposed to guarantee the procedure's safety. Furthermore, the thicker and straighter contrast flow was regarded as the indicator of successful decompression.[35,36,40,43–45] One article provided additional information regarding the appropriate quantity of contrast. It was described to be the least quantity of contrast necessary to provide sufficient views of the working space.[43] Moreover, some authors have reported that the number of levels and bilaterality could be determined intra-operatively based on epidurogram.[34]

However, the Motion study demonstrated that both epidurogram and usage of bony landmarks are acceptable for safety profile.[46] Furthermore, Pope et al strongly suggested that epidurogram was not necessary, and bony landmarks were safe enough for the *MILD* procedure.[38] The author retrospectively reviewed *MILD* cases with epidurogram (80 cases) and without epidurogram (67 cases) during the procedure. In both groups, nerve injury, hematoma, and other complications were not identified. However, the author did not compare the efficacy of the two groups. There is no article evaluating whether the use of epidurogram affects clinical efficacy.

Therefore, future clinical research is required in these respects.

Quantity of LF Debulked

The amount of removed LF tissue is a key consideration for *MILD* surgery. The amount of removed LF should be adequate to decompress the nerve tissue without compromising the integrity of the inner layer of LF for safety concerns. Few articles have described the quantity of debulked LF. According to reports, approximately three sets of three passes with different directions were necessitated. The decompression process was defined to be complete when no more LF tissue can be debulked and the tissue sculptor "fell in the channel".[37,46]

However, several articles have recommended epidurogram as an assessment tool. These articles have considered that contrast flow becoming thicker and straighter was an indication of adequate decompression.[36,41,45,47]

Bilateral Decompression or Ipsilateral Decompression?

For LSS patients with bilateral symptoms, the *MILD* procedure should be implemented bilaterally. However, for LSS patients with ipsilateral symptoms, relevant articles do not specify whether *MILD* treatment should be performed bilaterally or ipsilaterally.

According to reports, between 86.7% and 100% of participants were treated bilaterally.[35,40,48] The percentages of procedure levels treated bilaterally were 64.7%-97.7%.[34,36,43,47,49,50] As the proportion of LSS patients with bilateral symptoms was lower than the aforementioned proportion, it could be inferred that substantial cases with unilateral symptoms were given bilateral *MILD* procedures. Therefore, further clinical research is required to determine what degree of stenosis necessitates bilateral decompression despite the presence of unilateral symptoms, whether the efficacy of bilateral decompression is superior to that of ipsilateral decompression, and whether bilateral decompression should be considered a medical recommendation.

Efficacy of *MILD*

Pain Reduction

There are numerous clinical trials of *MILD*. All relevant articles have reported obvious pain reduction after *MILD* treatment.

In the MiDAS ENCORE study, the VAS scores were 7.7, 3.1, 3.3, and 3.6 for before-treatment, 6-month, 1-year, and 2-year follow-up, respectively.[51] Another prospective descriptive study is being conducted at 11 US sites. The study cohort included 58 *MILD* patients. The baseline average VAS score was 7.4 (95% CI ± 0.5) and then improved to an average of 4.5 (95% CI ± 0.8) at a 1-year follow-up, with an improvement of 2.9 points (95% CI ± 0.8).[50]

The Motion study is a rigorously designed study to testify to the effectiveness of *MILD*. The multi-centered RCT set *MILD* combined with conservative treatments (*MILD* + CMM group) as the experimental group, and conservative treatments alone (CMM-alone group) as the control group. Sixty-nine patients were enrolled in each group. The study further subdivided LSS pain into leg pain and low back pain.[52] The article found that the fluctuation of leg pain was consistent with low back pain. In the Motion study, for the *MILD* + CMM cohort, the NRPS was 7.56 ± 1.4 at baseline, 2.4 ± 2.6 for back pain at 6-month follow-up, 2.5 ± 3 for leg pain at 6-month follow-up, 2.3 ± 2.7 for back pain at 1-year follow-up, and 3.6 ± 3.1 for leg pain at 1-year follow-up.[52] Whereas for the CMM-alone group at 1-year follow-up, back pain and leg pain only experienced 0.46 ± 1.3 and 1.46 ± 2.1 reductions, respectively. The between-group difference was statistically significant.

In conclusion, the reported baseline average VAS scores were 6.3–9.6 and the final post-operative average VAS scores were 2.3–5.8.[34,36,40–43,45,47–49,51,52]

The Duration of Pain Relief

In the MiDAS ENCORE study, the VAS score was reported to be 7.7, 3.1, 3.3, and 3.6 for before-treatment, 6-month, 1-year, and 2-year follow-up, respectively.[51] The longest follow-up period was 5 years. However, for this retrospective observational study, only outcomes within 1 year were available.[48]

In Richard Lingreen's retrospective review, the reported VAS score after *MILD* treatment was 5.8 ± 2.5, which was a relatively high pain perception. However, there are two considerations. First, the baseline VAS was 9.6 ± 0.42, indicating that the recruited participants had a relatively serious condition. Second, the follow-up time was only one month.[40] This result cannot be deemed ineffective.

In conclusion, if the appropriate candidates were enrolled, the pain intensity was reduced by roughly half, and to a mild pain level with a VAS score of 3 to 4 post-operatively. According to the current literature, the pain-reduction effect lasted for 1 to 2 years post-operatively. Low back pain and leg pain can be relieved simultaneously and to a similar degree.

In conclusion, the post-surgery pain reduction effect could emerge as early as 6 weeks post-operatively and remain stable for 2 years postoperatively.[36,49,51]

Degree of Functional Improvement from *MILD*

For LSS, apart from pain perception, functional status impairment is another concern. All available studies have demonstrated obvious functional improvements. For the MiDAS ENCORE study, the baseline ODI was 53.0 ±12.9 and improved to 30.3 at the 2-year follow-up. It was a reduction of approximately 42.8%.[51] In a Motion study, for the *MILD* + CMM cohort, the ODI score was reduced from 55.3 ± 14.3 at baseline to 39.2 at 1-year follow-up.[52] Mekhail et al implemented a multi-centered prospective study with 58 participants. The baseline ODI score was 48.6 (95% CI ± 3.8) and then improved to 36.7 (95% CI ± 5.8) at 1-year follow-up.[34] In Nagy Mekhail's study, a more straightforward index was applied. In the study, standing time and walking distance were observed. Standing time was improved from 8 minutes at baseline to 56 minutes at the 12-month follow-up, whereas walking distance was improved from 246 feet at baseline to 3956 feet at the 1-year follow-up.

In summary, the reported baseline average ODI scores were 38.8–55.3, and the final post-operative average ODI scores were 27.4–39.8.[36,43,45,47,49–52] In conclusion, after *MILD*, similar pain conditions, the functional status would improve dramatically.

Effective Rate of *MILD*

Several articles have discussed the effective rate. Most articles defined a VAS score reduction of 2 points or more compared with pre-treatment as effective. Lora L. Brown reported an 88% effective rate during a 12-week follow-up.[36] In the MiDAS ENCORE study, the effective rates were 57.3% at 1-year follow-up and 71.7% at 2-year follow-up.[33,51] A multi-center prospective clinical study by Bohdan Chopko reported a 66.7% effective rate post-operatively.[45] In Bohdan Wolodymyr Chopko's study, if a 2-point or greater VAS reduction was deemed effective, the calculated effective rate was 75%.[41]

Some studies have focused on patients' walking ability improvements for effective rate evaluation. Richard Lingreen reported a retrospective study. In the study, 1/42 (3%) participants could walk more than 15 min before the procedure, and the number increased to 25/42 (60%) after the *MILD* procedure.[40] It can be inferred that 57.1% (24/42) of participants experienced dramatic symptom improvement, which could be regarded as effective.

The patient satisfaction rate was also the focus of some articles. The satisfaction rate was 74% in Nagy Mekhail's study and 76% in Sanghamitra Basu's study.[43,50]

Some articles have reported the percentage of subsequent surgeries after the *MILD* procedure. In the Motion study, at 1-year follow-up, only 5.8% of participants in the *MILD* + conventional treatment group had undergone additional spine surgery subsequently.[52] In other words, 94.2% of participants did not require additional spine surgery after the *MILD* procedure. In a retrospective study of 75 patients with a 5-year follow-up, only 9 (12%) patients required lumbar surgical decompression, while 59 (78.7%) patients did not receive further surgery treatments. Of the nine participants with surgery, two reported pain relief, one reported worsened pain, and three reported no pain relief.[48] These articles may shed light on the effective rate.

In conclusion, the effective rate of the *MILD* procedure was between 57.1% and 88%.

Effectiveness of *MILD* Compared with Other Treatments

There are two level 1 RCT studies, comparing *MILD* with ESI treatment. In Lora L. Brown's study, 38 participants were randomly assigned to receive either *MILD* treatment or ESI. At the 6-week follow-up, the percentage of participants with pain reduction (equal to or exceeding 2 points) was statistically significant in the *MILD* group than in the ESI group: 76.2% vs 35.3%, respectively. The VAS score in the *MILD* group significantly decreased from 6.3 at baseline to 3.8 at the 6-week follow-up and 3.4 at the 12-week follow-up. The ODI score decreased from 38.8 at baseline to 27.4 at the 6-week follow-up and 18.6 at the 12-week follow-up. The two outcomes of the ESI group improve significantly. However, only

within-group differences with statistical significance were observed. The between-group differences were not statistically significant.[36]

In the MiDAS ENCORE study, a total of 274 patients were enrolled and randomly assigned to the *MILD* and ESI groups, with 143 and 129 participants, respectively. In the 1-year follow-up between the *MILD* and ESI groups: the ODI responder was 58% vs 27.1%, the NPRS was 57.3% vs 27.1%, the ZCQ (symptom severity domain) was 51.7% vs 31.8%, the ZCQ (physical function domain) was 44.1% vs 17.8%, and the ZCQ (patient satisfaction domain) was 61.5% vs 33.3%. All between-group differences were statistically significant. Between the *MILD* and ESI groups, the ODI reduction was 16.2 ± 1.6 vs 4.5 ± 1.1, the NPRS reduction was 2.8 ± 0.3 vs 0.7 ± 0.2. The differences were all statistically significant.[33]

In summary, Lora L. Brown's study revealed that *MILD* was superior to ESI but without statistical significance. However, considering the small sample size of 38 participants, the sample size is insufficient to demonstrate the between-group statistical difference. Whereas the MiDAS ENCORE study is a multi-center RCT with a sample size of 274 patients. It can be concluded that *MILD* treatment can exert apparent superior efficacy over ESI in terms of both pain reduction and functional improvement.

There is currently no head-to-head comparison between *MILD* and other minimal invasive treatments.

Complications of *MILD*

Dural tears, massive intraoperative hemorrhage, epidural hematoma, nerve root injury, and surgical infection are commonly reported complications of spinal procedures.

For *MILD*, procedure-related complications were rare. There are reports of soreness at the surgical site[40] and minor postoperative bleeding.[33,45]

In conclusion, complications of the *MILD* procedure are rare and minor.

Discussion

To date, we have searched 17 clinical studies about *MILD* (Table 1). Among them, three of them are level 1 RCT clinic trials. All clinical trials have demonstrated efficacy compared with pretreatment conditions.

The Motion study set *MILD* combined with conventional conservative therapies as the experimental group and conventional therapies alone as the control group.[52] As with its rational study design, the Motion trial is regarded to provide strong evidence for the efficacy of *MILD*. The other two studies set ESI as the control group. The studies have demonstrated significant superiority of *MILD* over ESI, although one of them did not demonstrate statistical significance.[33,36] In conclusion, *MILD* is an effective treatment modality and the efficacy is superior over ESI. Furthermore, only minor complications were reported, and *MILD* is regarded to be a safe procedure.

Here are some explanations regarding the *MILD*'s mechanism. LF thickening and infolding are predominant factors for spinal stenosis.[13,14,53] The compression is more severe during the lumbar extension position because the LF infolding was more obvious.[17,18] In the *MILD* procedure, the outer layer of the LF was removed, even though the inner layer of LF remained, the LF is thinner, and the inward folding movement of LF during lumbar extension would be minor. This finding makes the spinal canal to be enlarged slightly. This theory is testified by the fact that post-procedure epidurogram demonstrated thicker and straighter contrast flow than pre-procedure.[41,45] Furthermore, a report argues that in LSS patients, small increments in LF hypertrophy may cause obvious symptoms, whereas very small amounts of LF resection can significantly relieve the symptoms.[34] It would be postulated that after the *MILD* procedure, the inward pressure towards the inside nerve tissue would be mitigated after a small amount of LF removal and a small enlargement of the spinal canal, even though no current clinical trial can testify to this presumption. By contrast, most conservative treatments such as ESI or oral medication, can only mitigate nerve root inflammation or stabilize the nerve tissue. However, the space accommodating the nerve tissue cannot be enlarged, nor can the compression pressure exerted over the nerve tissue remain unchanged. This mechanism could be the background mechanism underlying the superior efficacy of *MILD* over ESI.

There are some advantages of *MILD*. First, as only a small part of bone tissue is removed; the bilateral facet joint, the lamina, and surrounding ligaments are reserved; therefore, the *MILD* procedure does not affect spinal stability. This

Table 1 Summary of the reviewed articles

Study	Year	Study design	level of evidence	Numbar of participants treated	Outcomes	Follow-up period	Results	Complications	Conclusions
Brown LL et al[36]	2011	Single-center double-blind randomized controlled trial, *MILD* vs. ESI	Level 1	38 participants, 21 in the *MILD* Group and 17 in the ESI Group	VAS, ODI, ZCQ	12 weeks	For MILD patients, average VAS fell from 6.3 at baseline to 3.4 at 12-week follow-up (P < 0.0001). Average ODI was reduced from 38.8 at baseline to 18.6 at 12-week follow-up (P < 0.0018).An average ZCQ of 1.8 at 12-week follow-up was reported. At 12-week follow-up, patients treated with *MILD* reported significantly greater pain decrease (P < 0.0001), and significantly greater functional mobility improvement (P < 0.0018) than ESI patients.	No complications were reported.	This study demonstrated that in LSS patients suffering with neurogenic claudication, *MILD* provides statistically significantly better pain reduction and improved functional mobility vs. treatment with ESI.
MiDAS ENCORE study, 1 year results[33]	2016	Multi-center randomized controlled trial, *MILD* vs. ESI	Level 1	302 patients, 149 in the *MILD* Group and 153 in the ESI Group.	VAS, ODI, ZCQ	1 year	Averag ODI improved by 16.2 ± 1.6 for the *MILD* Group vs. 4.5 ± 1.1 for the ESI Group (P < 0.001). Average NPRS improved by 2.8 ± 0.3 for the *MILD* Group vs. 0.7 ± 0.2 for the ESI Group (P < 0.001). All 3 ZCQ domains demonstrated statistically significant superiority of *MILD* versus ESI. The ODI responder rate of 58% in the *MILD* group was higher than the responder rate of 27.1% in the ESI group (P < 0.001). There is no difference in safety between *MILD* and ESIs.	For 1 patient, intraoperative oozing was observed at the decompression site. Another patient, experienced postoperative pain possibly related to MILD that resolved within 3 days of the index procedure.	*MILD* is statistically superior to ESIs in the treatment of LSS patients with neurogenic claudication and verified central stenosis due to ligamentum flavum hypertrophy.

MiDAS ENCORE study, 2 years results[51]	2017	Multi-center randomized controlled trial, *MILD* vs. ESI	Level 1	302 participants,143 in the *MILD* Group and 131 in the ESI Group for statistical analysis.	NPRS, ODI, ZCQ	2 years	At 2 years, ODI improved by 22.7 points, NPRS improved by 3.6 points,and ZCQ symptom severity and physical function domains improved by 1.0 and 0.8 points, respectively (P < 0.001). No between-group comparison results at 2-year follow-up were mentioned in the article.	For 1 patient, intraoperative oozing was observed at the decompression site. Another patient, experienced postoperative pain possibly related to *MILD* that resolved within 3 days of the index procedure.	*MILD* is an excellent choice for first-line therapy for selected patients with central spinal stenosis suffering from neurogenic claudication symptoms with hypertrophic ligamentum flavum.
The MOTION Study[52]	2022	Randomized controlled trial, *MILD* + CMM Group vs. CMM Group	Level 1	138 patients with 69 patients in each group	NPRS, ODI, ZCQ	1 years	For *MILD* + CMM Group, ODI improvement was 16.16 ± 19.0. NRPS improvement was 2.3 ± 2.7 for back pain and 3.6 ± 3.1 for leg pain. Results from all primary and secondary outcome measures showed statistical significance in favor of *MILD* + CMM (P < 0.001).	No complications were reported.	*MILD* is a safe, durable, minimally invasive procedure that has been shown to be effective as an early interventional therapy for patients suffering from symptomatic lumbar spinal stenosis.
Pope, JE et al[38]	2021	Retrospective single-center cohort study, procedures utilizing epiduragrams vs. no epiduragrams	level 3	147 participants, with 80 in Epiduragram Group and 67 in Non-epiduragram Group.	procedure-relatedcomplications including nerve injury, hematoma, infection, death, or allergic reaction to contrast use.	3 months	No complications were reported for both the two Groups.	No complications were reported.	This study strongly suggests the use of an epidurogram is not necessary for the safe decompression of a patient with symptomatic spinal stenosis and neurogenic claudication utilizing percutaneous direct decompression.
Pryzbylkowski P et al[39]	2022	Retrospective single-center cohort study, comparing *MILD* after receiving ≤1 ESIs or ≥ 2 ESIs	level 3	145 patients with 75 patients receiving ≤1 ESIs and 70 patients receiving ≥ 2 ESIs	VAS	3 months	Average VAS at baseline was 7.81 ±1.38 for ≤1 ESI Group and 7.48 ±1.27 for ≥2 ESI Group. Average VAS at post-treatment was 4.83 ±2.59 for ≤1 ESI Group and 4.56 ±2.53 for ≥2 ESI Group. Improvements in VAS at follow-ups compared with baseline were significant in both groups. No statistically significant differences were found between the two groups.	No complications reported.	Multiple ESIs prior to *MILD* showed no benefit. A modified algorithm to perform *MILD* immediately upon diagnosis or after the failure of the first ESI is recommended.

(*Continued*)

Table 1 (Continued).

MiDAS I study[45]	2010	Multi-Center prospective descriptive study	Level 4	75 participants included.	VAS, ODI, ZCQ, SF-12v2® Health Survey	6 weeks	The average VAS was reduced from 7.3 at baseline to 3.7 at 6-week follow-up (P < 0.0001). The average ODI was reduced from 47.4 to 29.5 at 6-week follow-up (P < 0.0001). The ZCQ and SF-12v2® Health Survey were also improved (P < 0.001).	No complications reported.	The *MILD* procedure demonstrated efficacy in improving mobility and reducing pain associated with lumbar spinal canal stenosis.
Lingreen R et al[40]	2010	Retrospective Descriptive Study	Level 4	44 participants included.	VAS, markers of global function we	1 month	The average VAS was reduced from 9.6 ± 0.42 at pre-treatment to 5.8 ± 2.5 at post-treatment (P < 0.05). Pacentage of patients with the ability of walking over 15 min was 60% compared with 3% at pre-treatment. percentage of patients with the ability of standing over 15 min was 73% compared with 14% at pre-treatment.	Minor adverse events, soreness lasting 3.8 days was most frequently reported.	The *MILD* procedure appears to be a safe and likely effective option for the treatment of neruogenic claudication in patients who have failed conservative therapy and have ligamentum flavum hypertrophy as the primary distinguishing component of the stenosis.
Chopko BW et al[41]	2011	Prostective descriptive study	Level 4	14 participants included.	VAS, ODI	23.5 weeks	The average VAS was reduce from 7.61 ± 2.0 to 3.61 ± 2.9 after the treatment (P = 0.05). The average ODI was reduced from 50 to a postoperative average of 43.9, the difference was with no significant significance.	No complications reported.	This pilot series points to a potential new therapeutic option for LSS in high-risk surgical patients.
Mekhail N et al[50]	2011	Multi-center descriptive case series	Level 4	58 participants included.	VAS, ODI, ZCQ, SF-12v2® Health Survey	1 year	The average VAS was reduced from 7.4 (95% CI ± 0.5) at baseline to 4.5 (95% CI ± 0.8) at one-year post-treatment (P < 0.0001). The ODI was reduced from 48.6 at baseline to 38.7 at one-year post-treatment (P < 0.0001). Patients' satisfaction rate was 74%.	No complications reported.	This cohort study demonstrated continued excellent safety profile of the *MILD* procedure and equally important, showed long-term pain relief and improved functionality.

Basu S et al[43]	2011	Prospective Descriptive Case Series	Level 4	27 participants included.	VAS, ODI, ZCQ	6 months	The average VAS was reduce from 9.1 (95% CI ±0.59) at baseline to 3.9 (95% CI ±2.25) (P < 0.0001). The average ODI was reduce from 55.1 (95% CI±6.34) at baseline to 31.1 (95% CI ±9.29) at 6-month follow-up (P < 0.0004). The average ZCQ Patient satisfaction score was 1.86 at 6-month follow-up.	No complications reported.	In this series, mild has been shown to be asafe, effective, and cost-effective treatment for LSS patients with neurogenic claudication.
Mekhail N et al[34]	2012	Prospective descriptive case series	Level 4	40 participants included.	PDI and Roland-Morris, Walking Distance, Standing Time, and VAS	1 year	At 1-year follow-up, both PDI and Roland-Morris showed significant improvement of 22.6 points (P < 0.0001) and 7.7 points (P < 0.0001), respectively. Walking Distance, Standing Time, and VAS improvements were also statistically significant, increasing from 246 to 3,956 feet (P < 0.0001), 8 to 56 minutes (P < 0.0001), and 7.1 to 3.6 points (P < 0.0001)respectively.	No complications reported.	This study demonstrated significant functional improvement as well as decreased disability secondary to neurogenic claudication after *MILD* procedure.
Wong WH et al[42]	2012	Descriptive case series	Level 4	17 participants included.	VAS, ODI	1 year	The baseline mean VAS of 7.6 improved at 1 year after the procedure to 2.3, with an average percentage decrease of 70.0%. Average baseline ODI of 48.4 improved to 21.7 at 1 year, an improvement of 26.6 points.	No complications reported.	The *MILD* technique provides an attractive early option for the treatment of symptomatic lumbar spinal stenosis after failed injection therapy, but before more invasive surgical treatment.

(*Continued*)

Table 1 (Continued).

Deer TR et al[47]	2011	Prospective descriptive case series	Level 4	46 participants included.	VAS, ODI, ZCQ	1 year	VAS improved significantly from a mean of 6.9 (95% CI ± 0.6) at baseline to an average of 4.0 (95% CI ± 1.0) at one-year follow-up (P < 0.0001). ODI improved from a mean of 49.4 (95% CI ± 2.5) at baseline to 32.0 (95% CI ± 5.8) at one-year follow-up (P < 0.0001).Statistically significant improvements were achieved in all ZCQ domains.Overall Symptom Severity improved from a mean of 3.5 at baseline to 2.3 at one-year follow-up.	No complications reported.	The *MILD* procedure was a safe and effective procedure for symptomatic LSS. the efficacay can occurr as early as 12 weeks and maintained through one year.
Chopko BW et al[49]	2012	Multi-center prospective descriptive study	Level 4	45 participants included.	VAS, ODI, ZCQ	2 years	VAS from an average of 7.2 (95% CI ± 0.6) at baseline to a mean of 4.8 (95% CI ± 0.8) at 2-year follow-up, an improvement of 2.4 points (P < 0.0001). Seventy-one percent of the patients (responders) reported an improvement in VAS at 2 years compared with baseline. ODI values showed statistically significant improvement from baseline average of 48.4 (95% CI ±4.4) to an average at year 2 of 39.8 (95%CI ± 5.6), improving 8.6 points (P < 0.0001).	No complications reported.	*MILD* procedure can exert significant pain relief and improved functionality for certain symptomatic LSS patients.
Mekhail N et al[48]	2021	Retrospective longitudinal observational cohort study	Level 4	75 participants included.	Opioid medications utilization	The follow-up period for the long-term durability was 5 years. The follow-up period for pain relief and opioid medications was 1 year.	Three patients were lost to follow-up, three patients were deceased, and one patient resides outside of the United States. Nine patients out of 75 (12%) required open surgical decompression within the 5-year follow-up. Average NPRS was reduced from 6.7 ± 2.2 at baseline to 3.7 ± 2.8 at 1-year follow-up (P < 0.0001).The MME was reduced from 15.5 ± 35.6 at baseline to 7.4 ± 20.9 at 1-year follow-up (P = 0.0067).	11 Postprocedural pain, 1 Ecchymosis and 1 Allergic dermatitis were reported.	The mild procedure is durable over 5 years and may allow elderly patients with symptomatic lumbar spinal stenosis to avoid lumbar decompression surgery while providing significant symptomatic relief.

Abbreviations: MILD, minimally invsive lumbar decompression; ESI, epidural steroid injection; ZCQ, Zurich Claudication Questionnaire; CMM, nonsurgical conventional medical management; PDI, Pain Disability Index, ; RMQ, Roland-Morris Disability Questionnaire; CI, conficence interval; MME, Morphine Milligram Equivalent; NPRS, numerical pain rating scale;

argument is supported by the absence of reports of post-procedure lumbar instability in all clinical trials. Second, to expose nerve tissues during open decompression surgery or microscopic decompression surgery, epidural fat tissue and vascular tissue should be removed. Possible postoperative epidural hemorrhage, fibrocyte deposition, and inflammatory reaction may lead to subsequent epidural adhesion and possible post-operative pain.[54–56] For endoscopic decompression surgery, even with continuous water irrigation during the surgery, epidural hemorrhage and epidural adhesion may happen. However, in *MILD* surgery, the inner layer of LF remains intact, hence there is no interference with the microenvironment of epidural space. Therefore, there is no complication of epidural space hemorrhage and post-surgery epidural adhesion. Post-surgery neuropathic pain is supposed to be scarce. Third, no intra-spinal adhesion exists after *MILD*, hence there would be no interference with further possible surgeries.

The treatment for LSS should be ladder-like. Except for LSS participants with severe or progressive nerve functional impairment, such as cauda equina syndrome, or true muscle weakness, conservative treatments such as oral medication, physical therapy, and epidural space steroid injection, should be initially applied.[7,57] They are the first ladder treatment modalities. Because of the advantage of minimal invasiveness, non-interference with future surgery, effectiveness, low complication rate, and minimal invasive treatments are accepted as a preferable option for patients who failed conservative treatment. Minimal invasive treatments can be regarded as the second ladder treatment. We considered invasive decompression surgery with or without fusion as the third ladder, which should be for patients who failed first and second ladder invasive treatments. There is another rationality for this ladder-like treatment principle. LSS is a chronic disease that progresses very slowly. Most LSS patients have been reported to be treated conservatively, hence the symptoms would remain stable within two years.[58] In other words, there is a safe time window between the first and second ladder treatments. Even if the symptoms were not relieved through first and second ladder treatments, we argue that it is never too late to upgrade to open surgery. As stated previously, there is significant superiority of *MILD* over ESI. In addition to the *MILD* procedure's obvious efficacy, there are no apparent complications and no interference with further invasive surgeries. The *MILD* procedure is assigned to the second ladder treatment group.

There are Some Limitations to the *MILD* Procedure

As mentioned previously, after the procedure, the VAS score could be reduced by roughly half, and to a post-procedure VAS of approximately 3–4. However, a VAS score of around 3–4 indicates a moderate level of pain perception. The effective rate of the *MILD* procedure was reported to be 57.1%-88%. That is to say, a certain proportion of participants continue to experience moderate or greater pain after the *MILD* procedure. For these participants who did not respond to *MILD*, the underline reasons are postulated to be either insufficient decompression or neuropathological components already existed before the procedure, or some other unknown reasons. Mekhail et al conducted a retrospective observational study with 75 participants.[48] During the 5-year follow-up, nine (12%) participants who failed the *MILD* procedure underwent decompression surgery. Of the nine surgery participants, only two of them reported symptom improvements, three reported no symptom changes, one experienced worsened symptoms, and the remaining three participants lost follow-up. Despite the sparsity of these clinic data of this type, we can speculate that insufficient decompression exists in *MILD*; however, the proportion is very low. Neuropathological components could have existed before the procedure as the primary reason.

Another limitation is that the indication for *MILD* is relatively narrow. It is only indicated for LSS caused by LF hypertrophy. LSS caused by disc prolapse, facet joint hypertrophy, or intervertebral stenosis is not an indication. Patients with previous spine surgery of the same segment are also contraindicated.

Here are some future directions for *MILD*-related clinic research. Most studies had a follow-up period of 1–2 years. The long-term efficacy was unknown. Therefore, clinical trials with a 5-year follow-up period are necessitated. Furthermore, numerous minimal invasive treatments currently exist, such as lumbar spinous process spacer and endoscopic lumbar decompression. However, there is no research with a head-to-head comparison between these treatments. Further clinical trials in this regard are needed.

Conclusion

MILD can significantly reduce pain intensity and improve functional status. It is a safe procedure with no major procedure-related complications and has the advantage of minimal invasiveness and non-interference with future surgery. It is accepted as an option for LSS patients who failed conservative treatment, however its long term efficacy is still uncertain.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Katz JN, Zimmerman ZE, Mass H, Makhni MC. Diagnosis and management of lumbar spinal stenosis: a review. *JAMA*. 2022;327(17):1688–1699. doi:10.1001/jama.2022.5921
2. Walter KL, O'Toole JE. Lumbar Spinal Stenosis. *JAMA*. 2022;328(3):310. doi:10.1001/jama.2022.6137
3. Deer TR, Grider JS, Pope JE, et al. The MIST guidelines: the lumbar spinal stenosis consensus group guidelines for minimally invasive Spine treatment. *Pain Pract*. 2019;19(3):250–274. doi:10.1111/papr.12744
4. Lurie J, Tomkins-Lane C. Management of lumbar spinal stenosis. *BMJ*. 2016;352:h6234. doi:10.1136/bmj.h6234
5. Messiah S, Tharian AR, Candido KD, Knezevic NN. neurogenic claudication: a review of current understanding and treatment options. *Curr Pain Headache Rep*. 2019;23(5):32. doi:10.1007/s11916-019-0769-x
6. Manchikanti L, Knezevic NN, Boswell MV, Kaye AD, Hirsch JA. Epidural injections for lumbar radiculopathy and spinal stenosis: a comparative systematic review and meta-analysis. *Pain Physician*. 2016;19(3):E365–410. doi:10.36076/ppj/2016.19.E365
7. Costandi S, Chopko B, Mekhail M, Dews T, Mekhail N. Lumbar spinal stenosis: therapeutic options review. *Pain Pract*. 2015;15(1):68–81. doi:10.1111/papr.12188
8. Javid MJ, Hadar EJ. Long-term follow-up review of patients who underwent laminectomy for lumbar stenosis: a prospective study. *J Neurosurg*. 1998;89(1):1–7. doi:10.3171/jns.1998.89.1.0001
9. Zaina F, Tomkins-Lane C, Carragee E, Negrini S. Surgical versus non-surgical treatment for lumbar spinal stenosis. *Cochrane Database Syst Rev*. 2016;2016(1):CD010264. doi:10.1002/14651858.CD010264.pub2
10. Siebert E, Pruss H, Klingebiel R, Failli V, Einhaupl KM, Schwab JM. Lumbar spinal stenosis: syndrome, diagnostics and treatment. *Nat Rev Neurol*. 2009;5(7):392–403. doi:10.1038/nrneurol.2009.90
11. Kreiner DS, Shaffer WO, Baisden JL, et al. An evidence-based clinical guideline for the diagnosis and treatment of degenerative lumbar spinal stenosis (update). *Spine J*. 2013;13(7):734–743. doi:10.1016/j.spinee.2012.11.059
12. Schonstrom N, Lindahl S, Willen J, Hansson T. Dynamic changes in the dimensions of the lumbar spinal canal: an experimental study in vitro. *J Orthop Res*. 1989;7(1):115–121. doi:10.1002/jor.1100070116
13. Yamada H, Oya M, Okada T, Shiozawa Z. Intermittent cauda equina compression due to narrow spinal canal. *J Neurosurg*. 1972;37(1):83–88. doi:10.3171/jns.1972.37.1.0083
14. Hansson T, Suzuki N, Hebelka H, Gaulitz A. The narrowing of the lumbar spinal canal during loaded MRI: the effects of the disc and ligamentum flavum. *Eur Spine J*. 2009;18(5):679–686. doi:10.1007/s00586-009-0919-7
15. Schmid MR, Stucki G, Duewell S, Wildermuth S, Romanowski B, Hodler J. Changes in cross-sectional measurements of the spinal canal and intervertebral foramina as a function of body position: in vivo studies on an open-configuration MR system. *AJR Am J Roentgenol*. 1999;172 (4):1095–1102. doi:10.2214/ajr.172.4.10587155
16. Fujiwara A, An HS, Lim TH, Haughton VM. Morphologic changes in the lumbar intervertebral foramen due to flexion-extension, lateral bending, and axial rotation: an in vitro anatomic and biomechanical study. *Spine*. 2001;26(8):876–882. doi:10.1097/00007632-200104150-00010
17. Inufusa A, An HS, Lim TH, Hasegawa T, Haughton VM, Nowicki BH. Anatomic changes of the spinal canal and intervertebral foramen associated with flexion-extension movement. *Spine*. 1996;21(21):2412–2420. doi:10.1097/00007632-199611010-00002
18. Chung SS, Lee CS, Kim SH, Chung MW, Ahn JM. Effect of low back posture on the morphology of the spinal canal. *Skeletal Radiol*. 2000;29 (4):217–223. doi:10.1007/s002560050596
19. Kim J, Kwon WK, Cho H, et al. Ligamentum flavum hypertrophy significantly contributes to the severity of neurogenic intermittent claudication in patients with lumbar spinal canal stenosis. *Medicine*. 2022;101(36):e30171. doi:10.1097/MD.0000000000030171
20. Kim YU, Park JY, Kim DH, et al. The role of the ligamentum flavum area as a morphological parameter of lumbar central spinal stenosis. *Pain Physician*. 2017;20(3):E419–E424.
21. Muto M, Giurazza F, Guarnieri G, et al. Dynamic MR in patients affected by neurogenical claudication: technique and results from a single-center experience. *Neuroradiology*. 2016;58(8):765–770. doi:10.1007/s00234-016-1697-7
22. North RY, Li Y, Ray P, et al. Electrophysiological and transcriptomic correlates of neuropathic pain in human dorsal root ganglion neurons. *Brain*. 2019;142(5):1215–1226. doi:10.1093/brain/awz063
23. Kobayashi S, Kokubo Y, Uchida K, et al. Effect of lumbar nerve root compression on primary sensory neurons and their central branches: changes in the nociceptive neuropeptides substance P and somatostatin. *Spine*. 2005;30(3):276–282. doi:10.1097/01.brs.0000152377.72468.f4
24. Delamarter RB, Bohlman HH, Dodge LD, Biro C. Experimental lumbar spinal stenosis. Analysis of the cortical evoked potentials, microvasculature, and histopathology. *J Bone Joint Surg Am*. 1990;72(1):110–120. doi:10.2106/00004623-199072010-00018
25. Porter RW. Spinal stenosis and neurogenic claudication. *Spine*. 1996;21(17):2046–2052. doi:10.1097/00007632-199609010-00024
26. Kobayashi S, Takeno K, Miyazaki T, et al. Effects of arterial ischemia and venous congestion on the lumbar nerve root in dogs. *J Orthop Res*. 2008;26(11):1533–1540. doi:10.1002/jor.20696
27. Kobayashi S. Pathophysiology, diagnosis and treatment of intermittent claudication in patients with lumbar canal stenosis. *World J Orthop*. 2014;5 (2):134–145. doi:10.5312/wjo.v5.i2.134

28. Cowley P. Neuroimaging of Spinal Canal Stenosis. *Magn Reson Imaging Clin N Am*. 2016;24(3):523–539. doi:10.1016/j.mric.2016.04.009

29. Steurer J, Roner S, Gnannt R, Hodler J, LumbSten Research C. Quantitative radiologic criteria for the diagnosis of lumbar spinal stenosis: a systematic literature review. *BMC Musculoskelet Disord*. 2011;12:175. doi:10.1186/1471-2474-12-175

30. Andreisek G, Imhof M, Wertli M, et al. A systematic review of semiquantitative and qualitative radiologic criteria for the diagnosis of lumbar spinal stenosis. *AJR Am J Roentgenol*. 2013;201(5):W735–46. doi:10.2214/AJR.12.10163

31. Lafian AM, Torralba KD. Lumbar spinal stenosis in older adults. *Rheum Dis Clin North Am*. 2018;44(3):501–512. doi:10.1016/j.rdc.2018.03.008

32. Lee S, Lee JW, Yeom JS, et al. A practical MRI grading system for lumbar foraminal stenosis. *AJR Am J Roentgenol*. 2010;194(4):1095–1098. doi:10.2214/AJR.09.2772

33. Benyamin RM, Staats PS. MILD(R) is an effective treatment for lumbar spinal stenosis with neurogenic claudication: miDAS ENCORE randomized controlled trial. *Pain Physician*. 2016;19(4):229–242. doi:10.36076/ppj/2019.19.229

34. Mekhail N, Costandi S, Abraham B, Samuel SW. Functional and patient-reported outcomes in symptomatic lumbar spinal stenosis following percutaneous decompression. *Pain Pract*. 2012;12(6):417–425. doi:10.1111/j.1533-2500.2012.00565.x

35. Staats PS, Benyamin RM. MiDAS ENCORE: randomized controlled clinical trial report of 6-month results. *Pain Physician*. 2016;19(2):25–38. doi:10.36076/ppj/2016.19.25

36. Brown LL. A double-blind, randomized, prospective study of epidural steroid injection vs. the mild(R) procedure in patients with symptomatic lumbar spinal stenosis. *Pain Pract*. 2012;12(5):333–341. doi:10.1111/j.1533-2500.2011.00518.x

37. Deer T, Kim C, Wahezi SE, Qu H, Sayed D, Investigators MS. Objective real-world outcomes of patients suffering from painful neurogenic claudication treated with the mild((R)) procedure: interim 6-month report of a randomized controlled trial. *J Pain Res*. 2021;14:1687–1697. doi:10.2147/JPR.S312573

38. Pope JE, Deer TR, Falowski SM. A retrospective, single-center, quantitative analysis of adverse events in patients undergoing spinal stenosis with neurogenic claudication using a novel percutaneous direct lumbar decompression strategy. *J Pain Res*. 2021;14:1909–1913. doi:10.2147/JPR.S304997

39. Pryzbylkowski P, Bux A, Chandwani K, et al. Minimally invasive direct decompression for lumbar spinal stenosis: impact of multiple prior epidural steroid injections. *Pain Manag*. 2022;12(2):149–158. doi:10.2217/pmt-2021-0056

40. Lingreen R, Grider JS. Retrospective review of patient self-reported improvement and post-procedure findings for mild (minimally invasive lumbar decompression). *Pain Physician*. 2010;13(6):555–560.

41. Chopko BW. A novel method for treatment of lumbar spinal stenosis in high-risk surgical candidates: pilot study experience with percutaneous remodeling of ligamentum flavum and lamina. *J Neurosurg Spine*. 2011;14(1):46–50. doi:10.3171/2010.9.SPINE091012

42. Wong WH. mild Interlaminar decompression for the treatment of lumbar spinal stenosis: procedure description and case series with 1-year follow-up. *Clin J Pain*. 2012;28(6):534–538. doi:10.1097/AJP.0b013e31823aaa9d

43. Basu S. Mild procedure: single-site prospective IRB study. *Clin J Pain*. 2012;28(3):254–258. doi:10.1097/AJP.0b013e31822bb344

44. Deer TR, Kapural L. New image-guided ultra-minimally invasive lumbar decompression method: the mild procedure. *Pain Physician*. 2010;13(1):35–41. doi:10.36076/ppj.2010/13/35

45. Chopko B, Caraway DL. MiDAS I (mild Decompression Alternative to Open Surgery): a preliminary report of a prospective, multi-center clinical study. *Pain Physician*. 2010;13(4):369–378. doi:10.36076/ppj.2010/13/369

46. Jain S, Deer T, Sayed D, et al. Minimally invasive lumbar decompression: a review of indications, techniques, efficacy and safety. *Pain Manag*. 2020;10(5):331–348. doi:10.2217/pmt-2020-0037

47. Deer TR, Kim CK, Bowman RG, Ranson MT, Yee BS. Study of percutaneous lumbar decompression and treatment algorithm for patients suffering from neurogenic claudication. *Pain Physician*. 2012;15(6):451–460. doi:10.36076/ppj.2012/15/451

48. Mekhail N, Costandi S, Nageeb G, Ekladios C, Saied O. The durability of minimally invasive lumbar decompression procedure in patients with symptomatic lumbar spinal stenosis: long-term follow-up. *Pain Pract*. 2021;21(8):826–835. doi:10.1111/papr.13020

49. Chopko BW. Long-term results of percutaneous lumbar decompression for LSS: two-year outcomes. *Clin J Pain*. 2013;29(11):939–943. doi:10.1097/AJP.0b013e31827fb803

50. Mekhail N, Vallejo R, Coleman MH, Benyamin RM. Long-term results of percutaneous lumbar decompression mild((R)) for spinal stenosis. *Pain Pract*. 2012;12(3):184–193. doi:10.1111/j.1533-2500.2011.00481.x

51. Staats PS, Chafin TB, Golovac S, et al. Long-term safety and efficacy of minimally invasive lumbar decompression procedure for the treatment of lumbar spinal stenosis with neurogenic claudication: 2-year results of MiDAS ENCORE. *Reg Anesth Pain Med*. 2018;43(7):789–794. doi:10.1097/AAP.0000000000000868

52. Deer TR, Costandi SJ, Washabaugh E, et al. The MOTION study: a randomized controlled trial with objective real-world outcomes for lumbar spinal stenosis patients treated with the mild(R) procedure: one-year results. *Pain Med*. 2022;23(4):625–634. doi:10.1093/pm/pnac028

53. Katz JN, Harris MB. Clinical practice. Lumbar spinal stenosis. *N Engl J Med*. 2008;358(8):818–825. doi:10.1056/NEJMcp0708097

54. LaRocca H, Macnab I. The laminectomy membrane. Studies in its evolution, characteristics, effects and prophylaxis in dogs. *J Bone Joint Surg Br*. 1974;56B(3):545–550. doi:10.1302/0301-620X.56B3.545

55. Liu S, Pan G, Liu G, et al. Electrospun fibrous membranes featuring sustained release of ibuprofen reduce adhesion and improve neurological function following lumbar laminectomy. *J Control Release*. 2017;264:1–13. doi:10.1016/j.jconrel.2017.08.011

56. Ross JS, Robertson JT, Frederickson RC, et al. Association between peridural scar and recurrent radicular pain after lumbar discectomy: magnetic resonance evaluation. ADCON-L European Study Group. *Neurosurgery*. 1996;38(4):855–861. doi:10.1227/00006123-199604000-00053

57. Bussieres A, Cancelliere C, Ammendolia C, et al. Non-surgical interventions for lumbar spinal stenosis leading to neurogenic claudication: a clinical practice guideline. *J Pain*. 2021;22(9):1015–1039. doi:10.1016/j.jpain.2021.03.147

58. Deyo RA, Gray DT, Kreuter W, Mirza S, Martin BI. United States trends in lumbar fusion surgery for degenerative conditions. *Spine*. 2005;30(12):1441–1445. doi:10.1097/01.brs.0000166503.37969.8a