Scoping Review

Basivertebral Nerve Ablation for the Treatment of Chronic Low Back Pain: A Scoping Review of the Literature

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Background: Chronic low back pain is a leading cause of disability worldwide and its pathophysiology remains poorly understood, a problem exacerbated by the heterogeneity of the patient population with chronic low back pain. Although the intervertebral discs are often implicated in chronic low back pain, studies have demonstrated strong innervation of the vertebral endplates by the basivertebral nerve, therefore making it a possible target for ablation in the treatment of vertebrogenic chronic low back pain.

Objectives: This work reviews the current evidence for the efficacy and safety of basivertebral nerve ablation as a treatment modality for chronic low back pain, and discusses the possible study biases and gaps in the current knowledge to provide insight on future research.

Study Design: The authors registered with the Center for Open Sciences and followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses Extension for Scoping Reviews (PRISMA-ScR).

Setting: A private clinic.

Methods: This study was performed in accordance with the following 5-stage methodological framework for scoping reviews: (i) identifying the research question; (ii) identifying relevant studies; (iii) selecting studies; (iv) charting the data; and (v) collating, summarizing and reporting the results. Three databases (PubMed, Web of Science, Embase) were searched using the keywords "basivertebral", "nerve", and "ablation".

Results: From March 2002 to March 2022, a total of 47 articles were identified, of which 12 were included in this scoping review, based on the exclusion criteria described in Table 1.

Limitations: The limitations found were:
- A very specific chronic pain population is typically utilized for this intervention. The inclusion criteria leave many who experience chronic low back pain ineligible for the procedure.
- Study demographics need to be more diversified to truly represent the chronic low back pain population.
- There is a lack of true control groups due to high crossover rates in published studies.
- Very few high-level or long-term studies have been published.
- Funding for many of the studies published on the subject is industry-led (Table 6). With an already limited amount of published research, a need for out-of-industry funding is required to avoid any possibility of bias.

Conclusions: Current research has shown that basivertebral nerve ablation might be a promising treatment for chronic low back pain in patients exhibiting Modic type 1 or 2 endplate changes, while additional research on the association between Modic changes and low back pain is still needed to gain widespread use and acceptance of this new treatment modality. The introduction of new devices and a larger number of independent studies would greatly enhance the confidence in the outcomes reported with this treatment modality in order to ultimately benefit patients, clinicians, and society.

Key words: Ablation, basivertebral nerve, chronic low back pain, endplate degeneration, intraosseous nerves, Modic changes, radiofrequency, vertebrae

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Chronic low back pain is a disorder causing significant disability among millions of patients worldwide (1). Effectively diagnosing the root cause of chronic low back pain still remains a challenge due to the multiple factors that could play a part in its origins, such as psychosocial conditions (2), pain's subjective nature (3), central nervous system connectivity, and patient lifestyle choices (4). The standard treatment for chronic low back pain ranges from conservative interventions to invasive modalities that often result in either temporary relief or modest reductions in perceived pain and function.

Research into the anatomic and pathobiological understanding of vertebral endplate degeneration has led to the concept of a vertebrogenic pain model (5), as opposed to the typically accepted discogenic pain model (6,7). This model has recently gained popularity with evidence of the adjacent vertebral endplates playing a significant role in chronic low back pain (8,9), along with research describing the innervation of the vertebral body by nerves that enter posteriorly by way of the basivertebral foramen branching from the sinuvertebral nerve (10). Multiple independent studies have concluded that Modic type 1 and 2 changes are associated with, at least some types of, chronic low back pain (11-19), even though these findings have also been challenged by others (20), thereby warranting further research.

It is in light of these findings that the concept of radiofrequency ablation, using either laser or radiofrequency, of the basivertebral nerve to treat chronic low back pain in patients displaying Modic changes began to take hold (21,22). Being a relatively new spinal procedure for the treatment of chronic low back pain, and in view of the growing amount of research and trials on the topic, we sought to review the current evidence on the safety and outcomes of basivertebral nerve ablation for the treatment of chronic low back pain, with an emphasis on the possible bias and limitations, and need for further research.

Methods

This review was registered with the Center for Open Science (https://osf.io/rjy78/). It was reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses Extension for Scoping Reviews (PRISMA-ScR) (23) and followed the 5-stage methodological framework for scoping reviews by Arksey and O'Malley (24): (i) identify the research questions ; (ii) identify relevant studies; (iii) select stud-ies; (iv) chart the data; and (v) summarize the results. This scoping review attempts to answer why is basivertebral nerve ablation possibly useful for patients with chronic low back pain, as well as to define the possible limitations of the currently available literature. We used a keyword search in March of 2022 for studies published in English with a date range of 20 years. The relevant studies were identified from PubMed, Embase, and Web of Science. The following search terms were used: "basivertebral AND nerve AND ablation". Studies were selected when meeting the inclusion and exclusion criteria described in Table 1; Fig. 1 describes the process we used for study inclusion within this scoping review. The data extraction process was performed by 2 independent reviewers (KM and WS). Most of the outcomes reported included the Oswestry Disability Index (ODI), the visual analog scale (VAS), opioid usage, the Short Form 36 Health Survey Questionnaire (SF-36), the EuroQol 5 Dimension 5 Level (EQ-5D-5L) questionnaire, and patient satisfaction measured using Macnab's criteria.

Results

Following the search protocol detailed in Fig. 1, 12 of the full-text articles retrieved met the inclusion criteria. These studies are summarized in Tables 2 and 3, and described in more detail below.

The INTRACEPT® device (Relievant Medsystems, Inc.), the only device currently approved by the US Food and Drug Administration for basivertebral nerve ablation. The detailed procedure has been described in Fischgrund, et al (25) and can be summarized as follows: the patient is placed in a prone position and the location of the entry pedicle at each proposed treatment level is determined and marked using standard anatomic landmarks; then, under fluoroscopic guidance, an introducer cannula is introduced through the pedicle until a breach in the posterior vertebral wall is done via the trocar. The introducer trocar is then exchanged with a smaller cannula assembly facilitating the creation of the curved path to the predetermined location at the terminus of the basivertebral nerve. The radiofrequency probe is finally introduced and activated at a temperature of 85°C for 15 minutes to denature the basivertebral nerve.

The results of the first pilot clinical investigation were published by Becker, et al in 2017 (26). In their prospective, single-arm, multicenter pilot study, Becker, et al reported on the extrapedicular (32% of the levels accessed) and transpedicular approach (68% of the

levels accessed) to ablate the basivertebral nerve for the treatment of chronic back pain. Sixteen patients with chronic low back pain for more than 6 months and unresponsive to at least 3 months of conservative care underwent magnetic resonance imaging (MRI) to confirm Modic type 1 or 2 changes. The baseline ODI was 52 ± 13, while the 3-month follow-up significantly decreased to 23 ± 21 ($P < 0.001$). VAS at baseline was measured at 61 ± 22 mm compared to a 6-week follow-up decrease to 38 ± 30 mm and a 3-month follow-up measured at 45 ± 33 mm ($P < 0.05$). SF-36 Physical Component Summary at baseline was 34.5 ± 6.5 with a 6-week follow-up increase to 44 ± 11 and a 3-month increase to 41.7 ± 12.4 ($P = 0.03$) (Table 3). Near the end of the study, curved instrumentation permitting broader access from a transpedicular entry was made available, and the author reported an overall targeting success rate of 91%. Given the promise of the pilot study, several other studies were later published on the use of the INTRACEPT® device for basivertebral nerve ablation.

Fischgrund, et al (25) then published the results from a prospective, double-blinded, randomized, sham-controlled multicenter clinical trial. This is to date the only sham-controlled study published on the topic. The study enrolled 225 patients with chronic low back with Modic type 1 or 2 changes at 15 sites who met exacting inclusion criteria. Patients were randomized to either the treatment or sham arm at each site after the patient was placed under anesthesia. This study placed the patients that were in the sham arm through the same operating room protocols as well as the same overall duration to increase generalizability while only docking the introducer cannula and simulating ablation, and keeping follow-up and treatment physicians

different to maintain blinding. Treatment targeting for this study was considered successful on 89% of the patients and 94.6% of vertebral bodies. This study demonstrated an average reduction in ODI at 2 and 6-week follow-ups as well as at 3, 6, and 12-month follow-ups (Table 3). VAS reporting at 3-months showcased non-statistically significant data compared to the sham arm, but 6-month and 12-month follow-up data displayed statistically significant improvement ($P = 0.008$ and 0.038, respectively) compared to the sham arm. At the one-year point, patients were given the option to cross over, which led to 73% deciding to join the treatment arm.

Fischgrund, et al. (27) described improvements that were sustained through a 2-year follow-up. Due to the high cross-over rate, postoperative results were compared to baseline results, with each patient serving as their own control. For this open-label follow-up 2-year report, both the ODI and VAS significantly ($P < 0.001$) decreased at all time points (2 weeks, 6 weeks, 3 months, 6 months, 12 months, and 24 months) while the SF-36 physical component summary significantly increased at all time points ($P < 0.001$) (Table 3).

Table 1. *Inclusion and exclusion criteria.*

Inclusion criteria	Exclusion criteria
Studies on the topic of basivertebral nerve ablation (n = 47)	• Commentaries (n = 1) • Letters to the editor (n = 4) • Reviews (n = 9) • Conference abstracts (n = 15) • Studies in which ablation of a nerve other than the basivertebral was also performed (n = 2) • Animal studies (n = 3) • Full text not available (n = 1)

Fig. 1. *PRISMA-ScR Chart. Out of the three database searches, and after removal of the redundant publications, a total of 47 publications were found using the keywords "Basivertebral", "nerve", and "ablation" during the time period ranging from 3/7/2002 to 3/7/2022. After applying the inclusion and exclusion criteria described in Table 1, 12 publications were included in this scoping review.*
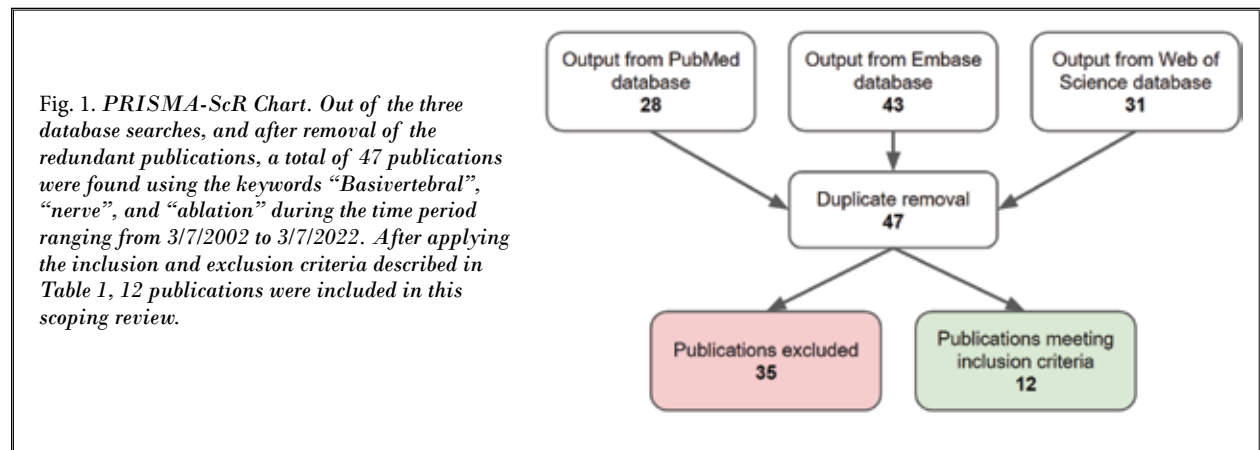
Table 2. *Summary of included publications.*

Authors	Patients	Study Design	Follow-up Period	Observations and Potential Limitations
Becker, et al 2017 (26)	17	Prospective, single-arm, multicenter (Pilot study)	Up to 12 months	Extrapedicular as well as transpedicular approaches. Subjects with Modic changes had optional discography, patients without Modic changes had mandatory discography. Industry funding.
Fischgrund, et al 2018 (25)	225	Prospective, randomized, double-blind, sham-controlled, multicenter (SMART trial)	Up to 12 months	Sham-controlled. Possible placebo effect. Baseline MRIs for Modic Type 1 or 2 changes. Industry funding. Commentary/critics published and answered (43,45).
Fischgrund, et al 2019 (27)	147	SMART trial follow-up	Up to 24 months	High crossover rate reported. Treatment arm compared to baseline. Industry funding.
Markman, et al 2020 (29)	77	SMART trial post hoc analyses	Up to 12 months	Inclusion of patients taking short-acting opioids. Self-reported patient outcomes. Industry funding.
Fischgrund, et al 2020 (28)	133	SMART trial follow-up	5+ years	Lack of a control group after patient cross-over. Self-reported patient outcomes. Industry funding.
Truumees, et al 2019 (30)	28	Prospective, open-label, single-arm, multicenter	Up to 6 months	Inclusion of patients using extended-release opioids and history of discectomy/laminectomy. Baseline MRIs for Modic type 1 or 2 changes. Self-reported patient outcomes. Industry funding.
Khalil, et al 2019 (31)	140	Prospective, multicenter, open label, randomized, controlled (INTRACEPT trial)	Up to 3 months	Basivertebral nerve ablation vs. standard care. Included patients using extended-release opioids and history of discectomy/laminectomy. Baseline MRIs for Modic Type 1 or 2 changes. Industry funding.
Smuck, et al (2021) (32)	140	INTRACEPT trial follow-up	Up to 12 months	Industry funding.
Koreckij, et al (2021) (33)	140	INTRACEPT trial follow-up	Up to 24 months	Industry funding.
Macadaeg, et al (2020) (34)	48	Prospective, single-arm, open label	Up to 12 months	Community practice setting. Wider inclusion criteria. Baseline MRIs for Modic Type 1 or 2 changes. Treatment of up to four vertebrae and treatment of nonconsecutive levels from L3 to S1. Self-reported patient outcomes. Industry funding.
Kim, et al 2018 (35)	14	Single-center, retrospective, observational study	Up to 20 months	No statistical analysis. Pfirmann's grading and Modic changes, discography. TELA (Lutronics) device. Targeted levels extended to L2-S1. Independently funded.
De Vivo, et al (2021) (36)	56	Prospective, experimental, uncontrolled trial	Up to 12 months	STAR™ Tumor Ablation System. SPEC/CT in addition to MRI for patients with Modic changes. Patients presented disc degeneration (Pfirmann's grading). European-based study. Patients with at least 6 weeks of failed conservative care. Independently funded. Commentary/critics published and answered (46,48).

Table 3. *Outcome details of included publications.*

Author(s)	Measured outcomes
Becker, et al. 2017 (26)	Oswestry Disability Index: 52 ± 13 pre-op, decreased to 23 ± 21 at 3 months ($P < 0.001$). Visual Analog Scale: 61 ± 22 mm pre-op, decreased to 38 ± 30 mm at 6 weeks, and to 45 ± 33 mm at 3 months ($P < 0.05$). SF-36 Physical Component Summary: 34.5 ± 6.5 pre-op, increased to 44 ± 11 at 6 weeks and 41.7 ± 12.4 at 3 months ($P = 0.03$).
Fischgrund, et al. 2018 (25)	Oswestry Disability Index: Pre-Op: 42.4 ± 10.92 per protocol (PP), 41.2 ± 10.38 sham arm, 3 months: PP reduced to 22.1 ± 15.39, sham arm reduced to 25.8 ± 17.44 ($P = 0.019$), 6 months: PP reduced to 21.6 ± 14.92, sham arm reduced to 25.1 ± 15.29 (N.S.), 12 months: PP reduced to 22.6 ± 15.71, sham arm reduced to 25.3 ± 14.92 (N.S.). Visual Analog Scale: Pre-Op: 6.73 ± 1.38 cm PP, 6.64 ± 1.34 cm sham arm, 3 months: PP reduced to 3.8 ± 2.63 cm, sham arm reduced to 4.14 ± 2.64 cm (N.S.), 6 months: PP reduced to 3.74 ± 2.68 cm, sham arm reduced to 4.41 ± 2.76 cm ($P = 0.008$), 12 months: PP reduced to 3.96 ± 2.83 cm, sham arm reduced to 4.46 ± 2.78 cm ($P = 0.038$). SF-36 Physical Component Summary: 3 months: PP least squares mean increased by 9.74, sham least squares mean increased by 9.05 (N.S.), 6 months: PP least squares mean increased by 10.2, sham least squares mean increased by 8.73 (N.S.), 12 months: PP least squares mean increased by 9.17, sham arm least squares mean increased by 7.63 (N.S.). SF-36 Mental Component Summary: 3 months: PP least squares mean increased by 2.24, sham arm least squares mean increased by 0.78 (N.S.), 6 months: PP least squares mean increased by 1.90, sham least squares mean increased by 1.17 (N.S.), 12 months: PP least squares mean increased by 1.13, sham least squares mean decreased by 1.46 ($P = 0.021$).
Fischgrund, et al 2019 (27)	Oswestry Disability Index: Preoperative: 42.4 ± 10.92, 2 weeks: decreased to 23.5 ± 15.41 ($P < 0.001$), 6 weeks: decreased to 23.1 ± 15.19 ($P < 0.001$), 3 months: decreased to 22.1 ± 15.39 ($P < 0.001$), 6 months: decreased to 21.6 ± 14.92 ($P < 0.001$), 12 months: decreased to 22.6 ± 15.71 ($P < 0.001$), 24 months: decreased to 18.8 ± 15.89 ($P < 0.001$). Visual Analog Scale: Preoperative: 6.73 ± 1.383 cm, 2 weeks: decreased to 3.74 ± 2.280 cm ($P < 0.001$), 6 weeks: decreased to 3.75 ± 2.532 cm ($P < 0.001$), 3 months: decreased to 3.80 ± 2.625 cm ($P < 0.001$), 6 months: decreased to 3.74 ± 2.684 cm ($P < 0.001$), 12 months: decreased to 3.96 ± 2.830 cm ($P < 0.001$), 24 months: decreased to 3.13 ± 2.636 cm ($P < 0.001$). SF-36 Physical Component Summary: Preoperative: 33.5 ± 7.366, 3 months: increased to 43.32 ± 9.481 ($P < 0.001$), 6 months: increased to 43.89 ± 8.686 ($P < 0.001$), 12 months: increased to 42.83 ± 9.199 ($P < 0.001$), 24 months: increased to 45.83 ± 9.216 ($P < 0.001$). Opioid Usage: 12 months: 60.7% of the patients who were taking opioids at the time of enrollment had reduced opioid medication, with 46.4% who completely stopped using.
Markman, et al 2020 (29)	Oswestry Disability Index: Treatment arm: patients who had decreased opioid use at 12 months: decrease of 24.9 ± 16.0 vs patients who had increased opioid use at 12 months: decrease of 7.3 ± 9.8 ($P < 0.001$). Sham arm: patients who had decreased opioid use at 12 months: decrease of 17.4 ± 16.1 vs patients who had increased opioid use at 12 months: decrease of 1.2 ± 14.3 (N.S.). Visual Analog Scale: Treatment arm: patients who had decreased opioid use at 12 months: decrease of 3.3 ± 2.7 cm vs patients who had increased opioid use at 12 months: decrease of 0.6 ± 1.8 cm ($P < 0.001$). Sham arm: patients who had decreased opioid use at 12 months: decrease of 2.5 ± 2.6 cm vs patients who had increased opioid use at 12 months: decrease of 1.4 ± 1.9 cm (N.S.).
Fischgrund, et al. 2020 (28)	Oswestry Disability Index: Preoperative: 42.81 ± 11.57, 5+ years: decreased by 25.95 ± 18.54 ($P < 0.001$). Visual Analog Scale: Preoperative: 6.74 cm, 5+ years: decreased by 4.38 ± 2.35 cm ($P < 0.001$). Patient Satisfaction: At 5+ years: 3% worsened condition, 27% unchanged, 70% improved.

Table 3 con't. *Outcome details of included publications.*

Author(s)	Measured outcomes

Truumees, et al. 2019 (30)	Oswestry Disability Index:
	  Pre-operative: 48.5 ± 10.42, 3 months: decreased to 30.07 ± 14.52 ($P < 0.0001$), 6 months (68% of the patients): decreased to 13.05 ± 11.99 ($P < 0.0001$).
	Visual Analog Scale:
	  Preoperative: 6.36 cm, 3 months: decreased to 2.86 ± 2.25 cm ($P < 0.0001$), 6 months (68% of the patients): decreased to 1.42 ± 1.77 cm ($P < 0.0001$).
	SF-36 Physical Component Summary:
	  Preoperative: 31.62 ± 6.69, 3 months: increased to 47.41 ± 9.50 ($P < 0.0001$).
	SF-36 Mental Component Summary:
	  Preoperative: 51.01 ± 11.47, 3 months: increased to 55.24 ± 9.64 ($P < 0.0001$).
	EQ-5D-5L:
	  Preoperative: 0.606 ± 0.010, 3 months: increased to 0.805 ± 0.114 ($P < 0.0001$).

Khalil, et al 2019 (30)	Oswestry Disability Index:
	  3 months: least squares mean decreased by 25.3 (29.6 to 21.0) in treatment arm vs 4.4 (8.7 to 0.2) in standard care arm ($P < 0.001$).
	Visual Analog Scale:
	  3 months: least squares mean decreased by 3.46 cm (4.10 to 2.82) in treatment arm versus 1.02 cm (1.66 to 0.37) in standard care arm ($P < 0.001$).
	SF-36 Physical Component Summary:
	  3 months: least squares mean increased by 14.021 (11.995–16.048) in treatment arm vs 2.114 (0.088–4.140) in standard care arm ($P < 0.001$).
	SF-36 Mental Component Summary:
	  3 months: least squares mean increased by 2.615 (0.450–4.781) in treatment arm vs 2.786 (-4.952 to -0.620) decrease in standard care arm ($P < 0.001$).
	EQ-5D-5L:
	  3 months: least squares mean increased by 0.1803 (0.1469–0.2137) vs 0.0135 (-0.0203–0.0472) in control ($P < 0.001$)
	Patient satisfaction:
	  3 months: 6% worsened, 16% unchanged, 78% improved.

Smuck, et al (2021) (32)	Oswestry Disability Index:
	  12 months: reduced by 25.7 ± 18.5 ($P < 0.001$).
	Visual Analog Scale:
	  12 months: reduced by 3.8±2.6 cm ($P < 0.001$).
	SF-36 Physical Component Summary:
	  Baseline: 32.1 ± 6.8, 12 months: 47.0 ± 9.9 ($P < 0.001$).
	SF-36 Mental Component Summary:
	  Baseline: 53.4 ± 9.5, 12 months: 54.4 ± 7.6 (N.S.).
	EQ-5D-5L:
	  Baseline: 0.61 ± 0.13, 12 months: 0.81 ± 0.16 ($P < 0.001$).

Koreckij, et al (2021) (33)	Oswestry Disability Index:
	  24 months: decrease of 28.5 ± 16.2 ($P < 0.001$).
	Visual Analog Scale:
	  24 months: decrease of 4.1 ± 2.7 cm ($P < 0.001$).
	SF-36 Physical Component Summary:
	  24 months: increase of 16.30 ± 10.32 ($P < 0.0001$).
	SF-36 Mental Component Summary:
	  24 months: decrease of 0.328 ± 9.38 (N.S.).
	EQ-5D-5L:
	  24 months: increase of 0.200 ± 0.164 ($P < 0.0001$).

Macadaeg, et al. (2020) (34)	Oswestry Disability Index:
	  12 months: reduced to 32.31 ± 14.07 ($P < 0.001$).
	Visual Analog Scale:
	  12 months: decreased to 4.31 ± 2.51 cm ($P < 0.001$).
	SF-36 Total Score:
	  12 months: increase of 26.27 ± 17.19 ($P < 0.001$).
	SF-36 Physical Component Summary:
	  12 months: increase of 17.53 ± 9.73 (P value not reported).
	EQ-5D-5L:
	  12 months: increase of 0.22 ± 0.15 ($P < 0.001$).

Table 3 con't. *Outcome details of included publications.*

Author(s)	Measured outcomes

Kim, et al. 2018 (35)	Visual Analog Scale:
	  7.79 ± 0.98 cm pre-op, decreased to 1.93 ± 1.39cm (*P* < 0.0001) at one week, to 2.21 ± 0.89 cm (*P* < 0.0001) at 3 months, final follow-up at 2.36 ± 1.01cm (*P* < 0.0001).
	MacNab's criteria:
	  50% excellent, 42.86% good, 7.14% fair.

De Vivo, et al. (2021) (36)	Oswestry Disability Index:
	  12 months: decrease by 32.4 points (decrease ranging from 6 to 42).
	Visual Analog Scale:
	  12 months: decrease by 4.3 cm (decrease ranging from one to 7.5 cm).

N.S.: Not significant.

Fischgrund, et al (28) was an open-label, 5-year follow-up from the original random controlled trial. ODI scores compared to preoperative (42.81 ± 11.57) were reduced to 25.95 ± 18.54 (*P* < 0.001), while VAS scores were reduced from 6.74 cm to 4.38 ± 2.35 cm (*P* < 0.001) at the 5-year mark. Seventy-percent of the patients reported their condition improved, 27% reported no change, and only 3% reported a worsening condition (Table 3).

Markman, et al (29), in their post hoc analyses of the previously described sham-controlled trial (25), evaluated if patients reporting reduced opioid use have superior functional outcomes following ablation (Table 3). Markman, et al (29) demonstrated that ODI at 12-month follow-up from opioid users who reduced their usage showed a mean reduction of -24.9 ± 16.0 compared to those who increased usage with a mean reduction of -7.3 ± 9.8 (*P* < 0.001). Actively treated patients reporting decreased opioid use had a mean improvement in VAS of 3.3 ± 2.5 cm compared to 0.6 ± 1.8 cm for patients reporting increased opioid use (*P* < 0.001). In the sham arm, the improvements in VAS were 2.5 ± 2.6 cm and 1.4 ± 1.9 cm for patients reporting decreased vs increased opioid use, respectively. The sham arm of the study failed to report significant differences in functional improvements. The authors concluded that in patients with chronic low back who use short-acting opioids, pain relief obtained after the ablation of the basivertebral nerve resulted in a reduction in opioid use.

Truumees, et al (30) performed a prospective, open-label, single-arm, multicenter study broadening the inclusion criteria to patients using extended-release opioids and allowing patients with discectomy/laminectomy, under certain conditions. Prior discectomy had, for example, been performed in 14.3% of the patients. Reported outcomes (Table 3) were positive with preoperative ODI scores at 48.5 ± 10.42, which were reduced to 30.07 ± 14.52 (*P* < 0.0001) at the 3-month follow-up and to 13.05 ± 11.99 (*P* < 0.0001) at the 6-month follow-up. VAS scores at baseline were 6.36 cm compared to a decrease to 2.86 ± 2.25 cm at the 3-month follow-up and to 1.42 ± 1.77 cm (*P* < 0.0001) at the 6-month follow-up. Physical Component Summary scores at baseline were 31.62 ± 6.69 with an increase to 47.41 ± 9.50 at the 3-month follow-up, with Mental Component Summary at baseline reported at 51.01 ± 11.47 with an increase at the 3-month follow-up to 55.24 ± 9.64 (*P* < 0.0001).

A second multicenter randomized controlled trial was performed, but in this instance to evaluate the clinical effectiveness of basivertebral nerve ablation compared to standard care for chronic low back pain. Khalil, et al (31), in their prospective, randomized, multicenter study of intraosseous basivertebral nerve with a 3-month follow-up, reported a mean ODI change of -25.3 in the treatment arm compared to -4.4 points in the standard care arm. Secondary outcome measures resulted in a VAS score of a least squares mean decreased by 3.46 cm in the treatment arm compared to 1.02 cm in the control arm (*P* < 0.001). Physical Component Summary result was a least squares mean increase by 14.021 in the treatment arm, compared to 2.114 in the control arm (*P* < 0.001). Mental Component Summary resulted in a least squares mean increase of 2.615 in the treatment arm compared to a 2.786 decrease in the control arm (*P* < 0.001). EQ-5D-5L scores resulted in a least squares mean increase of 0.1803 in comparison to 0.0135 in the control arm (*P* < 0.001) (Table 3). In the ablation arm, 78% of the patients rated their condition as improved, 16% reported no change, and 6% reported a worsened condition.

Twelve-month follow-up results of a full randomized trial, including 3-month and 6-month between-arm comparisons, 12-month treatment arm results, and 6-month outcomes of basivertebral nerve ablation in the former standard care arm were published

by Smuck, et al (32). Results from basivertebral nerve ablation were superior to standard care at 3 months for the primary endpoint (mean ODI reduction, difference between arms of -20.3 [CI -25.9 to -14.7 points; *P* < 0.001]), VAS pain improvement (difference of -2.5 cm between arms [CI -3.37 to -1.64, *P* < 0.001]) and quality of life outcomes. At 12 months, basivertebral ablation demonstrated a 25.7 ± 18.5 point reduction in mean ODI (*P* < 0.001), and a 3.8 ± 2.6 cm VAS reduction (*P* < 0.001) from baseline, with 64% demonstrating ≥ 50% reduction and 29% pain free. Similarly, the former standard care patients who elected basivertebral nerve ablation (92%) demonstrated a 25.9 ± 15.5 point mean ODI reduction (*P* < 0.001) from baseline. Interestingly, no significant differences in opioid use were observed at the 6-month follow-up in this study.

Koreckij, et al (33) then reported the 24-month results of the basivertebral nerve ablation arm of this study. At 24 months, ODI and VAS improved 28.5 ± 16.2 points (*P* < 0.001) and 4.1 ± 2.7 cm (*P* < 0.001), respectively. A ≥ 50% reduction in pain was reported in 72.4% of patients; 31.0% were pain-free at 2 years.

In an effort to test the clinical effectiveness of basivertebral nerve ablation in a community practice setting, Macadaeg, et al (34) in their prospective, single-arm, open-label study enrolled patients displaying symptoms of vertebrogenic pain and Modic changes. The protocol was revised to allow treatment of up to 4 vertebrae and treatment of nonconsecutive levels from L3 to S1. Mean reduction in ODI at 12 months was 32.31 ± 14.07 (*P* < 0.001). Mean VAS pain score decrease was 4.31 ± 2.51 cm at 12 months (*P* < 0.001). Similarly, both the SF-36 and EQ-5D-5L scores improved (26.27 ± 17.19 and 0.22 ± 0.15 increases, respectively [*P* < 0.001]).

Only 2 studies were performed in an independent manner with no industry funding. Kim, et al (35) published data from a single-center, retrospective, observational study on transforaminal epiduroscopic basivertebral nerve laser ablation. Fourteen patients with chronic low back pain for at least 6 months and unresponsive to at least 4 months of conservative care were given an MRI and provocative discography to confirm type 1 or 2 Modic changes. Intraoperative laser provocation of the basivertebral nerve of the vertebral body with Modic changes was also used. The VAS score decreased from 7.79 ± 0.98 cm to 1.93 ± 1.39 cm (*P* < 0.001) after a week. At the 3-month follow-up, patients reported a VAS of 2.21 ± 0.89 cm (*P* < 0.001) with a final follow-up score of 2.36 ± 1.01 cm (*P* < 0.001) (Table 3). Patient satisfaction measured by MacNab's criteria

resulted in 50% reporting excellent, 42.86% as good, and 7.14% as fair.

De Vivo, et al (36), in their prospective noncontrolled trial, emphasized the need to use more than a Modic type 1 or 2 change viewed on an MRI as the criterion for patient enrollment. All patients in this study underwent a maximum ablation time of 5 minutes using an articulating bipolar radiofrequency electrode (STAR™ Tumor Ablation System, Merit Medical), while the total procedure averaged 32 minutes under computed tomography guidance with simultaneous 3D reconstructions obtained intraoperatively. Targeting was confirmed a success at 100% via MRI during the one-month follow-up, while 12-month results yielded VAS and ODI scores reduced significantly from baseline. The VAS mean change was measured at -4.3 cm (range -7.5 to -1 cm), while the ODI score mean change was measured at -32.4 points (range -6 to -42). Clinical success was achieved with 54/56 patients in which ODI scores decreased more than 20 points. Single photon emission computed tomography/computed tomography (SPECT/CT) was used in this study to confirm the source of chronic low back pain, while being extremely sensitive for bone abnormalities and providing the ability to perform full body scans compared to traditional MRI.

Importantly, no deaths or serious adverse events were reported in any of these studies.

DISCUSSION

Low back and neck pain are among the conditions causing the highest expenditures in the US health care system (37). Basivertebral nerve ablation for the treatment of chronic low back pain is a relatively new technique, with a limited number of publications available on the topic.

Only 12 full-text papers that provided clinical outcomes data were found and included in this scoping review. Thirty-five out of the original 47 search outputs (Fig. 1) were excluded from this scoping review, based on the exclusion criteria described in Table 1. It is noteworthy that Kim, et al (38,39) reported on radiofrequency ablation of both the sinuvertebral and basivertebral nerves in relation to its effect on pain score, disability score, and patient outcomes. Despite being interesting in the fact the authors used a different device than most studies included in this scoping review, these studies were excluded because it targeted both the basivertebral nerve and sinuvertebral nerve, using an approach for which safety may be more dif-

ficult to achieve than with an intraosseous approach. The emphasis on paravertebral muscle spasm in these studies was also a finding usually not reported when using the intraosseous procedure.

Our scoping review seems to indicate that basivertebral nerve ablation might be a promising and long-lasting intervention in the treatment of chronic low back pain. However, significant limitations have been noted by the various authors of the included studies, which emphasizes the need for further research. Most studies are indeed often limited to a very specific group of patients with chronic low back pain who need to meet certain exacting criteria (such as, for example, skeletally mature patients, 6 months of chronic low back pain, the presence of a type 1 or 2 Modic change, the absence of opioid dependency, depression and obesity, among other criteria), thereby leaving a large percentage of chronic pain sufferers to investigate more traditional options for pain management. Some studies included in this review used discography as a criterion to include patients (26,35), even though this technique has also faced some controversy (40,41). Most studies used MRI to include patients with Modic changes (Table 3), while De Vivo, et al (36) mentioned the need to include more than one source of imaging to diagnose/include patients and suggested that a comparative analysis of CT, MRI, and SPECT/CT would be the most effective manner of obtaining a reliable diagnosis. Pfirrmann grading has also been used in some studies (Table 3), and additional research would be needed to study pre-Modic changes and the link between Pfirrmann's grading and the potential benefits of basivertebral nerve ablation for chronic low back pain relief.

Demographically, white patients are also disproportionately represented in the published material, making up as much as 90% of the study population (42). Disparities between study designs, targeting, approach, the use of control groups and sham arms, inclusion and exclusion criteria, and outcome measures were also noted.

Some of these limitations and possible concerns have also been the object of 2 letters to the editor (43,44), which we considered important to mention for the sake of objectivity, even though they were excluded from this scoping review (as per exclusion criteria in Table 1). Concerns were voiced by Li, et al (43) over the work of Fischgrund, et al 2018 (25), mostly regarding the optimal anatomical location of the probe to target the basivertebral nerve at the S1 level, concerns which

were answered by Fischgrund in 2019 (45). Finally, several methodological concerns were voiced by Arana, et al (44) over the work of De Vivo, et al (36). Among others, concerns were made about the possible lack of association between Modic changes and low back pain in the southern European population (20), the inclusion and exclusion criteria, and the possible high exposure of patients to radiation during the SPECT/CT procedure. De Vivo, et al published their answers to these critics in 2022 (46). Most importantly, there is a paucity of independently funded studies, since most of the ones included in this scoping review made use of the INTRACEPT® system. Only 2 other studies made use of a different device. While it is worth mentioning that others are being developed, such as the Abbott Corporation's IonicRFTM device (47), De Vivo, et al's study (36) was based in Europe where the INTRACEPT® device is not available, and they therefore made use of a Merit Medical's STAR™ for radiofrequency ablation of the basivertebral nerve, in a procedure were the ablation takes only 5 minutes vs. the 15 minutes commonly needed by INTRACEPT® system users. Kim, et al (35) used a laser-based device instead of radiofrequency (transforaminal epiduroscopic laser ablation [TELA] Lutronics). This study was also set apart by the use of a laser instead of radiofrequency, an epidural approach, and the extended targeted level range (from L2 to S1). Since Modic changes have been observed as high as T12 (48,49), further research is necessary to determine if extending the range of vertebrae targetable for basivertebral nerve ablation could be of benefit to some patients with chronic low back pain caused by segments outside of the L3-S1 levels.

CONCLUSION

Current research has shown that basivertebral nerve ablation might be a promising treatment for chronic low back pain in patients exhibiting Modic type 1 or 2 endplate changes, with evidence suggesting better outcomes compared to standard care. Additional research on the association between Modic changes and low back pain, with a focus on the specific characteristic of each study sample, is however still needed to gain widespread use and acceptance of this new type of treatment (20). The introduction of new devices and a larger number of independent studies would also greatly enhance confidence in the outcomes reported with this treatment modality, since it has been a long-held principle that the outcomes from research should be consistently replicated in

clinical practice, and to ultimately benefit patients, clinicians, and society (50).

Implications for Research and Practice
- A minimally invasive intervention option for patients with chronic low back pain and Modic changes.
- A reduction in postoperative care and recovery time.
- A possible reduction in opioid usage, although further research is needed on this topic.

Limitations
- A very specific chronic pain population is typically utilized for this intervention: the inclusion criteria leave many who experience chronic low back pain ineligible for the procedure.
- Study focus has been made primarily for the same demographic population.
- Variability in inclusion criteria can make outcome comparisons difficult/impossible.
- There is a lack of true control groups due to high crossover rates in some published studies.
- Very few long-term studies have been published.
- Industry funding has dominated most published studies.

Further Research is Still Warranted to:
- Investigate the association between Modic chang-

es and chronic low back pain in specific populations to increase our knowledge on the sources of chronic low back pain
- Foster our understanding on the role of the sinuvertebral nerve and the basivertebral nerve on chronic pain
- Study pre-Modic chronic low back pain, for example using Pfirrmann's grading system, to better screen for patient inclusion and to better identify the specific level to target
- Basivertebral nerve ablation is currently only approved for L3-S1 in the United States. Additional studies evaluating the benefit of this treatment modality (possibly from T12 to S1) could benefit a broader patient population
- Most studies have excluded patients with preexisting surgery. There is a need to study the possible benefit of basivertebral nerve ablation to treat adjacent level disease postfusion
- Additional clinical trials should consider the randomization of patients between conservative care, basivertebral nerve ablation, and lumbar fusion, with the possibility for a crossover from the basivertebral nerve ablation group to the lumbar fusion group for patients with persistent symptoms
- Additional devices need to be developed and made widely available (not only in the United States).

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