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Review Article

Nonsurgical treatments for patients with radicular pain from lumbosacral disc herniation

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Abstract

BACKGROUND CONTEXT: Lumbosacral disc herniation (LDH) is one of the most frequent musculoskeletal diseases causative of sick leave in the workplace and morbidity in daily activities. Nonsurgical managements are considered as first line treatment before surgical treatment.

PURPOSE: This clinical practice guideline (CPG) is intended to provide physicians who treat patients diagnosed with LDH with a guideline supported by scientific evidence to assist in decision-making for appropriate and reasonable treatments.

STUDY DESIGN/SETTING: A systematic review.

PATIENT SAMPLE: Studies of human subjects written in Korean or English that met the following criteria were selected: patients aged ≥18 years, clinical presentation of low back and radicular leg pain, diagnosis of LDH on radiological evaluation including computed tomography or magnetic resonance imaging.

OUTCOMES MEASURES: Pain and functional evaluation scales such as visual analogue scale, numeric rating scale, and Oswestry disability index

METHODS: The MEDLINE (PubMed), EMBASE, Cochrane Review, and KoreaMed databases were searched for articles regarding non-surgical treatments for LDH published up to July 2017. Of the studies fulfilling these criteria, those investigating clinical results after non-surgical treatment including physical and behavioral therapy, medication, and interventional treatment in terms of pain control and functional improvements were chosen for this study.

RESULTS: Nonsurgical treatments were determined to be clinically effective with regards to pain reduction and functional improvement in patients with LDH. Nevertheless, the evidence level was generally not evaluated as high degree, which might be attributed to the paucity of well-designed randomized controlled trials. Exercise and traction were strongly recommended despite moderate level of evidence. Epidural injection was strongly recommended with high degree of evidence and transforaminal approach was more strongly recommended than caudal approach.

CONCLUSIONS: This CPG provides new and updated evidence-based recommendations for treatment of the patients with LDH, which suggested that, despite an absence of high degrees of evidence level, non-surgical treatments were clinically effective.

Keywords: Lumbosacral; Disc herniation; Nonsurgical; Treatment; Pain; Function

Introduction

Lumbosacral disc herniation (LDH) is a very common spinal disorder leading to lower back pain (LBP) and radicular leg pain [1,2]. This condition is defined as a displacement of disc components (nucleus pulposus or annulus fibrosis) beyond the intervertebral disc space [3]. Back and/or radicular leg pain caused by mechanical and chemical irritation of nervous tissues by herniated disc material is an important cause of disability and morbidity, which can lead to absence from work, burden on health-care resources, and other societal costs [4].

Nonsurgical managements are considered as firstline treatment. Although so many nonsurgical treatment methods have developed and been used in clinical practice, unsatisfactory clinical results are sometimes produced. Moreover, there are variable and inconsistent opinions about clinical efficacy or usefulness of each treatment method. In this regard, much discrepancy about decision-making of appropriate treatment for individual patients' exists among physicians. Thus, the development of a clinical practice guideline (CPG) by extensive literature review is clinically important because it will provide a reasonable and scientific basis for deciding treatment, which ideally will promote patients' quality of life, quality of medical service, and national health care.

The purpose of this CPG is to provide physicians who treat patients diagnosed with LDH with a guideline supported by scientific evidence to assist in decision-making for appropriate and reasonable treatments. This CPG is expected to help determine treatment options, improve clinical outcome, and reduce the extravagant costs to patients and health care.

Material and methods

Key questions

Three divisions were made for nonsurgical treatments: physical and behavioral therapy, medication, and interventional treatment. Key Questions (KQ) was established based on PICO (patients, intervention, comparison, and outcome). P consisted of adult patients diagnosed with LDH following clinical and radiological evaluation. O was clinical outcome including pain control and functional improvement. The number of KQs was mainly determined by the number of I, which included bed rest, heat therapy, electrical therapy, exercise, manual therapy, and traction in the division of physical therapy and nonsteroidal anti-inflammatory drugs (NSAID), systemic steroids, antidepressants, anticonvulsants, and opioids in the division of medications. In the division of interventional treatment, three subgroups including epidural injection, percutaneous epidural neuroplasty(PEN), and other interventions were established. Five KQs were formulated in the epidural injection subgroup, considering that epidural injection was performed using various approaches with variable injectate options and the comparison between the different treatment methods had clinical implications for physicians: clinical efficacy of epidural injection, comparison of clinical efficacy between the transforaminal and interlaminar approach, comparison of clinical efficacy between transforaminal and caudal injections, comparison of clinical efficacy with or without steroids, comparison of clinical efficacy between particulate and nonparticulate steroids. One KQ was formulated in the subgroup of PEN and other interventions, respectively. Among other intervention subgroups, various intervention treatments including nucleoplasty, percutaneous decompression, dorsal root ganglion neuromodulation by pulsed radiofrequency, and intradiscal electrotherapy were initially included. However, given that these procedures are not usually performed at the Departments of Physical and Rehabilitation Medicine in our country (at your institution?) and were recently replaced by other minimally invasive surgical techniques, only pulsed radiofrequency neuromodulation to the dorsal root ganglion was finally included in the analysis after discussion by the committee. Finally, six, five, and seven KQs were formulated for physical and behavioral therapies, medications, and interventional treatments, respectively.

Search strategy and selection criteria

We included studies of human subjects written in Korean or English that met the following criteria: patients aged ≥18 years, clinical presentation of low back and radicular leg pain, and diagnosis of LDH on radiological evaluation including computed tomography or magnetic resonance imaging (MRI). Exclusion criteria included previous history of lumbosacral surgery, nonspecific LBP without a definite diagnosis of LDH on radiological evaluation, severe spinal stenosis, severe disc degeneration (Pfirmann Grade IV and V), intradiscal derangement or a bulging disc, and prominent spinal instability. Of the studies fulfilling these criteria, those investigating clinical results of nonsurgical treatment in terms of pain control and functional improvements were chosen for this study. This process was done adhering to PRISMA guideline, which was demonstrated as flow chart of Appendix 2 (please note if PRISMA guidelines were adhered to—it seems they were).

Database search and study extraction

The MEDLINE (PubMed), EMBASE, Cochrane Review, and KoreaMed databases were searched for articles published up to July 2017. We established individual search terms in each database's search engine (Appendix 1). The search was not restricted to randomized controlled trials (RCT) and was extended to original articles, including systematic reviews (SR) and non-RCTs. The decision to include an article was primarily made based on title and abstract review, followed by full-text inspection. Study screening and data extraction were independently performed by two reviewers, and any discrepancies were resolved by discussion between the two reviewers or with the committee members.

Quality assessment of selected studies, establishment of level of evidence, and strength of recommendation

Quality assessment of each study and level of evidence (LoE) was established in accordance with the Grading of Recommendations Assessment, Development and Evaluation methodology [5]. Of the selected studies, a RCT was considered first in quality assessment. The bias assessment for each RCT was conducted using the risk of bias (ROB) method, which consisted of seven domains: random sequence generation, allocation sequence concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting, and other biases. Recently published SR, which analyzed RCTs were also included in the quality assessment and were evaluated using the Assessment of Multiple Systematic Review. The quality of the SR was graded as high (score 9–11), moderate (score 5–8), and low quality (score 0–4) [6].

In the absence of an RCT or SR suitable for the KQ, a non-RCT was considered as a candidate in the quality assessment. The bias for each non-RCT was assessed by the Risk of Bias Assessment tool for Nonrandomized Study, which consisted of the following domains: comparability of participants, selection of participants, confounding variables, intervention (exposure) measurements, blinding outcome assessment, outcome evaluations, incomplete outcome data, selective outcome reporting, and other biases. All the domains were evaluated as "low risk," "high risk," or "unclear." These evaluations were performed by two independent reviewers and disagreements were resolved by discussion between the two reviewers or with the committee members.

Considering comprehensively the components of inconsistency, indirectness, imprecision, and publication bias in addition to ROB of all studies, the LoE was determined as high, moderate, low, or very low grade. The strength of recommendation (SoR) was determined as strong or weak by comprehensively assessing not only the evidence level, but also by other factors including balancing advantages and disadvantages, resources required, values and preferences, and acceptability/feasibility [5,7]. The LoE and SoR were determined by discussion with the entire committee members.

Results

Flow charts describing process of article selection for each KQ are shown in Appendix 2 and a summary table of selected articles is presented in Appendix 3.

Physical and behavioral therapy

1. Bed rest is not recommended for patients with radicular pain due to LDH because it does not show better clinical efficacy for pain reduction or functional improvement than continuation of activities (LoE: low, SoR: weak).

Two RCTs revealed that bed rest showed no better or slightly worse clinical efficacy than maintenance of normal daily activities, which was not statistical significant [8,9]. The LoE was determined as low grade due to high ROB and inaccuracy. Although bed rest was easily adopted in patients with acute pain, bed rest did not help to enhance clinical efficacy and in addition delayed the return to work or daily activities [8,10]. This lowered the preference in the patients as well as physicians. Accordingly, SoR was determined to be weak.

2. Heat therapy is recommended in patients with radicular pain due to LDH because it shows clinical efficacy, including pain reduction and functional improvement (LoE: very low, SoR: weak).

The RCT comparing the clinical efficacy of traction, ultrasound, and lower powered laser showed that no significant difference was observed among the three treatment groups, whereas all groups achieved significant pain reduction and functional improvement [11]. Due to a high ROB and inaccuracy, the LoE was assessed as very low grade. Because heat therapy had more benefits over harmful effects and could be applied with good accessibility and low cost, the patients and physicians had good preference for heat therapy. Only one study provided a very low LoE; therefore, the SoR was determined to be weak.

3. Electrical therapy is inconclusive as treatment for patients with radicular pain due to LDH (LoE: very low, SoR: inconclusive).

One RCT comparing the clinical efficacy of transcutaneous electrical nerve stimulation with vertebral axial decompression therapy indicated that while decompression produced successful pain reduction in 68.4% of patients, transcutaneous electrical nerve stimulation obtained successful pain reduction in 0% of patients [12]. The LoE was determined as very low because of the very high ROB and inaccuracy. Although electrical therapy had the advantage of good accessibility or applicability and was assumed to have more benefits over adverse effects (AE), one RCT provided a negative result with a low LoE. Thus, it was concluded that electrical therapy was inconclusive as a treatment method for patients with LDH.

4. Manual therapy is recommended in patients with radicular pain due to LDH because it shows clinical efficacy including pain reduction and functional improvement (LoE: very low, SoR: weak).

Three RCTs were finally selected, which supported the clinical efficacy of manual therapy. Manual therapy showed superiority in pain reduction and waist flexion angle improvement to conventional physical therapy [13]. Active manipulations had more effects than simulated manipulations on pain relief for acute back pain and sciatica with LDH, even though there were no significant better improvements on quality of

life and psychosocial scores [14]. Besides, manual therapy could obtain more significant pain reduction at 2 and 4 weeks than chemonucleolysis, but not at 12 months [15]. With the comprehensive consideration of these studies' results, manual therapy could be recommended. However, selected studies were conducted using different comparison treatments and with a small number of patients. Therefore, strength of the recommendation was weak due to the very low LoE resulting from inconsistency, indirectness, and inaccuracy.

5. Exercise is recommended in patients with radicular pain due to LDH because it shows clinical efficacy including pain reduction and functional improvement (LoE: moderate, SoR: strong).

One RCT conducted a cross-study with dividing patients into groups A and B. Both groups showed significant improvement in pain scores, straight leg lifting, and time required to perform specific tasks after 4 weeks of exercise. Notably, group A maintained the improvement of clinical parameters obtained by exercise until 4 weeks after cessation of exercise [16]. Due to inaccuracies because of the small number of patients, the LoE was evaluated as moderate. Exercise had predominantly more benefits than harmful effects and could be conducted not only in the clinic but also at the gym, and even in private spaces without any additional costs. Thus, preference was very high in patients and physicians. In this regard, this could be considered a high SoR.

6. Traction is recommended in patients with radicular pain due to LDH because it shows clinical efficacy including pain reduction and functional improvement (LoE: moderate, SoR: strong).

One study suggested that traction showed additional advantages to physical therapy [17]. Traction showed superiority in terms of pain and functional scores, the Shober test, and H-reflex than in controls [18], and revealed better MRI findings than medication at 2 months after treatment, despite no advantages of pain score reduction [19]. A SR concluded with moderate degree of evidence that traction had additional short-term effects when combined with medication and electrotherapy [20]. The LoE was determined to be of moderate degree because of the inconsistency of the methods used across the selected RCTs, although one SR was rated as high quality. Nevertheless, traction was regarded as having an advantage over harmful effects and was preferred by patients and physicians. Traction also had good applicability and accessibility. Traction has a strong recommendation level.

Medication

1. NSAIDs are recommended in patients with radicular pain due to LDH because these agents show clinical efficacy in pain reduction and functional improvement (LoE: low, SoR: weak).

Among the three RCTs, despite two studies reporting NSAIDs showed better pain reduction than placebo up to 7 days after beginning treatment [21,22], one study showed that NSAIDs did not obtain more pain reduction than placebo [23]. One SR also stated no significantly better clinical efficacy by NSAIDs in terms of pain reduction than placebo and represented the LoE as low grade due to the high ROB and inaccuracy in addition to the lack of remarkable effects [24].

NSAIDs were clinically effective in patients with LDH; thus, these agents could be recommended. However, their benefits compared with placebo were not very high based on the results from selected studies. Due to a serious ROB and inaccuracy validated in one of the selected RCTs, the evidence level was determined to be low, although the SR was rated of high quality. Clinical benefits over AEs could not be ascertained to be of a high degree because side effects including gastrointestinal AEs, cardiotoxicity, or hepatotoxicity were observed [25–27]. However, accessibility was regarded as very high and NSAIDs could be taken with low medical costs. In consideration of these advantages and limitations, NSAIDs could be recommended in patients with LDH, but the SoR was evaluated as weak.

2. Systemic steroids are recommended in patients with radicular pain due to LDH because they show clinical efficacy including pain reduction and functional improvement (LoE: low, SoR: weak).

The SR reported that the systemic administration of steroids was not useful as patients taking systemic steroids showed no better pain control, a higher frequency of surgery, and a higher incidence of side effects [28]. Nevertheless, three RCTs reporting their results after the SR had been published indicated the positive effects of systemic steroid. More pain reduction could be achieved by systemic dexamethasone in patients visiting the emergency unit with acute lumbosacral radicular pain, although this clinical benefit was diminished 6 months after treatment [29]. In addition, more functional improvement could be obtained by taking oral steroids for 15 days with tapering, although no significantly better pain control could be achieved [30]. More effective pain reduction was shown to occur in patients treated with oral triamcinolone for 14 days than with and oral anticonvulsant [31]. Overall, the administration of systemic steroids elicited clinical benefits, allowing their recommendation, although the LoE was estimated as low grade due to the low accuracy resulting from the small number of patients and inconsistencies from the variable types of steroid used, the variable follow-up period, and the heterogeneity of subjects across the selected RCTs. The SoR was also evaluated as weak due to the low LoE and concerns for possible side effects related to systemic steroids.

3. Opioids are recommended in patients with radicular pain due to LDH because it shows clinical efficacy including pain reduction and functional improvement (LoE: low, SoR: weak).

A RCT comparing the clinical efficacy of tapentadol and the combination tapentadol and pregabalin demonstrated that both groups obtained significant pain reduction but a statistically significant difference was not found between the groups. The incidence of AEs including dizziness or sedation was significantly lower in the tapentadol group [32]. The other RCT showed that the morphine and paracetamol groups showed better pain control than the placebo group, and the morphine group also showed superior results to the paracetamol group [33].

Opioid was regarded to be effective in pain control and hence could be recommended for patients with LDH. However, the LoE was determined to be of low grade because of the high ROB and inconsistency of methodology used in selected studies. The SoR was weak because of concerns of addiction and the low LoE. (This is a sensitive topic in the US and elsewhere—any comment on duration of opioids from the literature reviewed? There were no comments about duration of opioids or addiction in two RCTs selected.)

4. The clinical efficacy of anticonvulsants in terms of pain reduction and functional improvement has been inconclusive to date for treating patients with radicular pain due to LDH (LoE: moderate, SoR: inconclusive).

One RCT showed that leg pain could be reduced by a mean of 19% and global pain relief was shown to be significantly more distinguished with use of topiramate than with diphenhydramine, but side effects and dropouts were more frequent with topiramide. The study did not recommend topiramate unless studies of alternative regimens showed a better therapeutic ratio [34]. Gabapentin also failed to show better clinical effects than placebo [35]. The combination of tapentadol and pregabaline showed no additional clinical efficacy over the tapentadol alone, but resulted in more frequent side effects [32]. It was demonstrated that even if most patients with chronic lumbosacral radiculopathy responded to pregabalin therapy, the time to loss of response after discontinuation of drug did not significantly differ between pregabalin and placebo [36].

The LoE was regarded as moderate due to study inaccuracies, despite well-designed blind randomized studies. The clinical advantage of anticonvulsants was not distinctly better than placebo or opioids, although risk of side effects was reported to be considerable. The recommendation for use of anticonvulsant therapy in the treatment of patients with LDH could not be conclusively determined.

5. Antidepressants are recommended in patients with radicular pain due to LDH because it shows clinical efficacy including pain reduction and functional improvement (LoE: low, SoR: weak).

Nortriptyline, morphine, and their combination might not have significantly better clinical results than active placebo for the treatment of chronic sciatica [37]. Milnacipran produced a significant reduction in radicular pain and LBP than placebo [38]. Moreover, duloxetine could also achieve significantly more pain reduction than placebo at 4 weeks follow-up [39]. Hence, antidepressants could be recommended in patients with LDH. The LoE was evaluated as low grade because of potential inaccuracies due to small sample size and inconsistencies in clinical effects and type of agents. The SoR was also determined to be weak because of concerns of AEs and low LoE.

Interventional treatment

With regards to epidural injection, our database search yielded 9088 articles initially. After removing 2,377 duplicates, the total number of potentially eligible articles was 6,711. After screening abstracts and titles, 6,407 articles were excluded leaving 304 articles to be retrieved for further analysis. Of these, 221 were subsequently excluded because they did not satisfy the inclusion criteria. Among the 83 articles remaining, the articles appropriate for each of the five KQs were chosen individually.

1. Epidural injection is recommended in patients with radicular pain due to LDH because it shows clinical efficacy including pain reduction and functional improvement (LoE: high, SoR: strong).

Five SRs that were finally chosen concurred that epidural injection was effective in patients with LDH with high LoE [40–44]. Although the short-term clinical effects were supported by strong evidence, the long-term effects were less strongly supported [41,44]. The selected SRs were all evaluated as high quality. Besides the high LoE presented by relevant studies, epidural injection could be strongly recommended given its many advantages in the clinical practice setting; clinical benefits over the risk of AEs were expected to be high. Applicability or accessibility was good because the devices required for epidural injection including C arm fluoroscopy were readily available even in primary clinics in South Korea. Epidural injection could play a role in significantly decreasing the requirement of more expensive and invasive procedures by obtaining clinical results with easier and less invasive methods in patients' refractory to other conservative managements [43].

2. Transforaminal epidural injection has a higher recommendation than interlaminar epidural injection for treating patients with radicular pain due to LDH because transforaminal injection shows better clinical efficacy including pain reduction and functional improvement

than interlaminar injection (LoE: moderate, SoR: weak).

Among the eight RCTs and one SR selected, no significant difference in clinical efficacy was found between the transforaminal and interlaminar approaches in four studies [45–48], although the other four studies reported that transforaminal injection obtained significantly better clinical effects during the 3- to 12-month follow-up period than interlaminar injection [49–52]. One article noted that transforaminal injection was more effective in the short-term but this superiority diminished after 2 weeks of treatment [53]. Transforaminal injection could be more highly recommended than interlaminar injection considering the superior clinical outcomes supported by selected studies and as well as no higher cost, resources, and equipment.

The LoE was determined to be of moderate degree due to inconsistencies of design or methodology across RCTs, although one SR was assessed as high quality. The SoR was determined as weak, given that in addition to the not high LoE, inconsistent superior results in selected RCTs, and the more frequent reports of pain or discomfort during transforaminal injection than interlaminar injection.

3. Transforaminal epidural injection is more highly recommended than caudal epidural injection in treating patients with radicular pain due to LDH because transforaminal injection shows better clinical efficacy including pain reduction and functional improvement than caudal injection (LoE: moderate, SoR: strong).

Three of four RCTs indicated that transforaminal injection accomplished significantly higher clinical efficacy than caudal injection [50–52], whereas only one study reported the opposite result [54]. Clinical outcomes were significantly better in cases of spreading of contrast media into ventral epidural spaces than into dorsal epidural spaces after transforaminal injections. Therefore, the better outcomes of transforaminal approach may be attributed to the ability of this approach to infuse the treatment into the ventral epidural space, which is considered the main pain generator [51].

The LoE was regarded as moderate degree because of inconsistencies in doses or types of medications used in studies. Despite the evidence level being not relatively high, the transforaminal injection was more strongly recommended than caudal injection because in addition to dominantly better clinical results found in selected RCT, no additional costs or equipment were required.

4. Epidural injection with steroids is more recommended than without steroids for treating patients with radicular pain caused by LDH because epidural injection with steroid injection shows better clinical efficacy in terms of pain reduction and functional improvement (LoE: low, SoR: weak).

Although one RCT and one SR demonstrated that steroid injection had no more significant clinical benefits than injection of normal saline or local anesthetics [55,56], three RCT showed that steroid lead to significantly better clinical outcomes [57–59]. Two studies stated that the superior result of steroids was restricted only to the short term [58,59]. Epidural injection with steroids could be recommended because steroid showed at least comparable or additional effects. The cost of steroids was not burdensome and was easily accessible in the clinical setting, and furthermore, if used prudently, local administration was expected to have less harmful systemic AEs than systemic administration [60,61]. Nonetheless, the LoE was evaluated to be of low grade as the number of subjects in the selected RCT was small and overall the studies did not reveal any consistent evidence supporting the advantage of steroids due to heterogeneous methodology and study design. Moreover, there is currently ongoing debate regarding the advantages of steroids over concerns about AEs after repetitive steroid injections [62]. Conclusively, the use of epidural injections might be more recommended, albeit with weak SoR.

5. Epidural injection with particulate steroid is not recommended for treating patients with radicular pain due to LDH because epidural injection with particulate steroid does not achieve better clinical efficacy in terms of pain reduction and functional improvement than nonparticulate steroid (LoE: low, SoR: weak).

The three RCTs identified did not show any consistent results. One RCT stated that particulate steroid achieved better results in pain reduction but not in functional improvement [63]. Another reported no superior results for particulate steroid than for nonparticulate steroid [64]. The third RCT suggested that nonparticulate steroid obtained better functional improvement at the 6-month follow-up, even though no significant differences were observed between both types of steroid at the 3-month follow-up [65]. Two SRs recommended nonparticulate steroid be used in epidural injection because nonparticulate steroid showed comparable clinical efficacy with less probability of AEs [66,67]. Serious AEs including neurologic deficits resulting from spinal cord infarct following inadvertent intravasation of particulate steroid have been reported. Hence, administration of particulate steroid during spinal procedures is illegal in South Korea.

In conclusion, epidural injection with particulate steroid was not recommended, although with weak strength because the LoE supported by the identified studies was low due to a high degree of bias and inconsistency in study methods and design.

6. The clinical efficacy of PEN in terms of pain reduction and functional improvement is inconclusive to date for

treating patients with radicular pain due to LDH. (LoE: very low, SoR: inconclusive)

PEN, also called as neurolysis or adhesiolysis, is an epidural procedure using a catheter, which is inserted and placed into the ventral epidural space of the target lesion site. This approach removes epidural adhesion or tethering of the nerve root and thereafter delivers medication into the lesion site more directly and effectively. Overall, PEN contributed to clinical improvements in LDH patients, considering the results of studies published hitherto [68–71].

However, the LoE was evaluated as very low grade because of high ROB of non-RCTs. Along with a very low grade of evidence, uncertainty as to whether the benefits overwhelmingly surpass the risk or burdens associated with PEN lead to reluctance in making a decision regarding the recommendation level. The probability of side effects after PEN includes vascular injury, arachnoiditis, infection, or dural tear because the catheter was inserted and manipulated inside of the epidural space [72]. These properties of PEN decreased the accessibility or feasibility of the primary clinic toward PEN. Hence, it was inconclusive whether PEN could be recommended in treating patients with LDH. Comparative studies with other treatment modalities including epidural injection were required in the future.

7. Pulsed radiofrequency (PRF) neuromodulation to the dorsal root ganglion is recommended in patients with radicular pain due to LDH because it shows clinical efficacy including pain reduction and functional improvement (LoE: moderate, SoR: weak).

One RCT did not observe significantly better clinical outcomes in those treated with PRF as compared with patients treated transforaminal epidural injection [73]. The other RCT supported the clinical usefulness of PRF in patients with LDH [74]. PRF modulation achieved useful clinical results, despite no significant superiority to epidural injection.

The LoE was measured as moderate due to inaccuracy. Although PRF neuromodulation required additional equipment and costs associated with PRF, the procedure could be conducted with relatively simple methods, similar to transforaminal injection, which would allow easy accessibility to the primary clinic. This would also prevent repetitive steroid injections, which might lead to systemic side effects. In conclusion, PRF neuromodulation to dorsal root ganglion could be recommended with weak strength.

Discussion

This CPG suggests that nonsurgical treatment could produce clinical improvement in LDH, so that nonsurgical treatment should be considered and attempted before decisions for surgical treatment [75].

Although physical therapy or medications have represented the most popular treatment tool for LDH patients from tertiary care hospitals to primary clinics, there is limited literature available, especially with regards to RCTs evaluating physical therapy or medications. Moreover, the selection of only patients with LDH, and excluding other spinal pathologies including stenosis or degenerative disc diseases, further reduced the number of suitable RCTs eligible for this CPG. In clinical practice, physical therapy or medication is provided, based on the patients' clinical symptoms rather than on a specific diagnosis. Consequently, most reports on physical therapy or medication include patients with LBP in general instead of a specific disease such as LDH diagnosed by radiological evaluation [76–81]. These constraints contributed to the reduction of evidence level by not providing sufficient evidence to support physical therapy and medication.

Nevertheless, the lowered evidence level did not necessarily mean that physical therapy and medication were not useful treatments. According to Grading of Recommendations Assessment, Development and Evaluation system that we chose for evaluation tool in this CPG, SoR was determined not only by the evidence level, but also by other various factors including balancing advantages and disadvantages, resources required, values and preferences, and acceptability/feasibility [5]. Thus, although a treatment tool was evaluated to have weak statistical or clinical significance, it could be determined to be recommendable treatment strategy through discussion of committee members.

Heat therapy succeeded in obtained meaningful clinical improvement in pain and functional measurement as much as other physical modalities, in spite of showing no superiority to other modalities [11]. Heat therapy was regarded as clinically useful treatment method, given that it produced clinical benefits and was easily used with low cost and good accessibility. Manual therapy was supported by three RCTs showing that manual therapy showed significantly better clinical scores than other treatment methods [13–15]. Four weeks of exercise sessions also produced significant improvement than same period without exercise [16]. Traction was revealed to be better than control and no inferior to physical therapy or medication, which was usually regarded as useful treatment methods for LDH by physicians [17–19]. Thus committee members came to a conclusion that manual therapy, exercise and traction were worthy of being recommended in spite of relatively low level of evidence, taken that they produced meaningful clinical benefits, could be easily accessed, and preferred by physicians as well as patients.

The clinical advantages of NSAIDs and systemic steroid over placebo were supported by RCTs [21,22,29,30], Single use of opioid showed better clinical outcome than opioid plus anticonvulsant or acetaminophen, evidenced by RCTs [32,33]. Antidepressant also had more advantages in pain reduction than placebo according to RCTs [38,39]. These results enabled committee members to recommend these medications even with low strength because of relatively low LoE from shortcomings of studies' quality.

Epidural injection was supported by a high LoE, and thus was strongly recommended. There was criticism regarding epidural injection in that its clinical efficacy was diminished over time and could not be prolonged. However, clinical data at long-term follow up after epidural injection were difficult to be responsible for previously performed epidural steroid injection because the effects substantially deteriorated over this duration [82–84]. The main goal of epidural injection was to control pain rapidly rather than to anticipate long lasting effects [82]. Therefore, physicians should not be discouraged from performing epidural injections due to concerns of the limitations of its long-term effects. About 2–3 sessions per year usually achieved satisfactory results, and once a successful result was obtained, other strategies including exercise and lifestyle modifications to maintain the clinical benefits obtained through epidural injection should subsequently be considered [85–88]. Experimental study revealed that exercise and physical activity could maintain spinal health for a long time by attenuating fibrotic alterations of multifidus muscle associated with disc degeneration [89].

An interesting aspect regarding epidural injections was which technique would be more beneficial. This CPG indicated that the transforaminal approach be more recommended than the interlaminar approach with weak strength, and then the caudal approach with strong strength. Because the radicular pain originated from chemical irritation around the nerve root sheath or the dorsal root ganglion, the degree of perineural spread was a key factor in effectively reducing radicular pain. The transforaminal approach was more target-specific in the dorsal root ganglion or nerve root than the caudal or interlaminar approaches, which allowed the transforaminal approach to better control radicular pain [90–92]. Recently published two meta-analyses by same first author also indicated that transforaminal approach was significantly better in clinical outcomes than caudal or interlaminar approach in patients with LDH [93,94].

This CPG had several limitations. First, meta-analysis was not performed; thus, statistical significance could not be assessed. Second, mainly due to the limited literatures available, comparative questions between different the treatments strategies were insufficiently provided, although this would be useful information for clinicians who treated patients with LDH.

In conclusion, nonsurgical treatments including physical and behavioral therapy, medication, and interventions were clinically effective in patients with LDH diagnosed using clinical and radiological approaches including computed tomography and MRI. Despite the relatively low LoE, overall favorable results might encourage physicians to choose a nonsurgical method when treating patients with LDH. It was notable that epidural injections were reputed to have a high degree of evidence and strong recommendation. Despite their greater invasiveness than physical therapy, successful clinical outcomes achieved by epidural injections could lessen the possibility for performing more extensive or invasive surgery.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.spinee.2019.06.004.

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