

Efficacy and safety of proprioceptive neuromuscular facilitation for chronic low back pain: A meta-analysis of randomized controlled trials

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ABSTRACT

Objectives: This study aimed to evaluate the effectiveness and safety of proprioceptive neuromuscular facilitation for chronic low back pain.

Materials and methods: Eleven databases were searched from their inception through January 2021. The primary outcomes were pain intensity, individual activities, quality of life, and adverse events.

Results: Four randomized controlled trials (RCTs) with 184 patients (mean age: 37.8±3.1 years; range, 35 to 50 years) met the inclusion criteria. The pooled effect size showed proprioceptive neuromuscular facilitation, relieved pain (standard means difference [SMD]: -0.835, 95% CI: -1.139 to -0.531, p<0.001, n=4), and improved individual activity (Roland Morris Disability Questionnaire, SMD: -1.765, 95% CI: -2.642 to -0.888, p<0.001, n=2; Oswestry Disability Index, SMD: -0.893, 95% CI: -1.434 to -0.352, p=0.001, n=1) for chronic low back pain (CLBP).

Conclusion: This study verified that proprioceptive neuromuscular facilitation could relieve pain and improve individual activities without serious adverse events in patients with CLBP; however, it should be cautiously recommended due to the small number of included RCTs.

Keywords: Chronic low back pain, meta-analysis, proprioceptive neuromuscular facilitation, systematic review.

Chronic low back pain (CLBP) is defined as local pain from 12 ribs to the subgluteal fold for more than three months, commonly with no specific pathology.^[1] The prevalence of CLBP is about 23% worldwide^[2] and even double that in Japan.^[3] Chronic low back pain develops usually based on the recurred acute low back pain (about 25 to 50% per year).^[4] It is one of the most common skeletal muscle problems, which mainly limits the range of waist motion, decreases strength, endurance, and flexibility of the trunk muscles,^[5] results in depression, anxiety,

and disability,^[6-8] and in turn, it has placed a heavy burden on patients, communities, and the global economy.^[9-11] The common conservative managements of CLBP include modalities with heat, ultrasound, electrical stimulation, and physical therapies, such as traction, joint mobilization, manipulation, massage, and exercise.^[12] Interestingly, proprioceptive neuromuscular facilitation (PNF) therapy has been applied for CLBP in recent years.^[13-16] Proprioceptive neuromuscular facilitation was primarily developed by Dr. Herman Kabat and his collaborators in 1940s^[17] and

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is used for numerous neurologic and musculoskeletal diseases.^[18] It was reported that PNF could promote neuromuscular responses through stimulating proprioceptors,^[19,20] improve muscular strength,^[21,22] joint stability, mobility,^[23-27] neuromuscular control, and coordination, consequently improving the overall functional ability of patients with CLBP.^[28-30] However, the evidence on PNF for the management of CLBP is not sufficient.^[20] Thus, the present study was conducted to assess the effectiveness and safety of the PNF for CLBP.

MATERIALS AND METHODS

Search strategy

Eleven databases were electronically searched (PubMed, Science Direct, Wiley Online Library, EBSCO, Web of Science, Ovid, Cochrane Library, and Embase; CNKI, VIP, WanFang) from their inception through January 24, 2021. The search on PubMed used the following index formula: (“pnf” OR “proprioceptive neuromuscular facilitation”) AND “back pain” OR “protrusion of intervertebral disc” OR “lumbar muscle degeneration” OR “CLBP” OR “lumbar spine” OR “low back pain”) AND (“randomized controlled trial” OR “RCT” OR “controlled”). Other studies were collected through manual searches of reference lists in relevant literature reviews. The search strategy was designed by two authors and performed independently; if discrepancies were to occur, a consensus was reached through discussion. If multiple studies conducted by the same researchers were retrieved, the papers that had detailed data were included. The published languages were limited to English and Chinese.

Inclusion and exclusion criteria

All retrieved articles were evaluated independently by two reviewers (LXL and KYH) according to the following criteria: (i) patients: all of the participants had been clinically diagnosed as CLBP; (ii) interventions: PNF; (iii) comparison: PNF vs. routine medical care, conventional rehabilitation, sham PNF, or blank control; (iv) outcomes: the primary outcomes included pain intensity, individual activities, health-related quality of life (HRQOL), and safety assessments; (v) study design: randomized controlled trials (not including quasi-randomized controlled trials). Exclusion criteria were as follows: (i) nonoriginal research articles (e.g., letters, conference abstracts, comments, case reports, reviews); (ii) full text or

data unavailable; (iii) published in a language other than English or Chinese.

Data extraction

Following the inclusion and exclusion criteria, the eligible studies were elaborately evaluated, and the data were extracted independently by two authors. Data related to the following information was collected: author, year, sample size, age, sex, duration, PNF protocols, and outcomes related to pain intensity, individual activities, HRQOL, and safety assessments. If detailed information on the extracted data was necessary, the authors of the included studies were contacted. Differences and contradictions were resolved by discussion between the two authors.

Quality assessment

Two reviewers evaluated independently the quality of the methodology with the Physiotherapy Evidence Database (PEDro) scale (<https://www.pedro.org.au/>).^[31] The PEDro scale consists of 11 items with the scores (from 0 to 10). Ten items involve methodological quality related to statistical report (i.e., random assignment, covert assignment, baseline comparability, blind subjects, blind therapist, blinded evaluator, adequate follow-up and treatment intention analysis, comparison between groups and point estimates, and variability) and one item (qualification criteria) related to external validity, which is not included in the total scores. The PEDro scores of ≥ 7 were considered to be high quality, scores of 5 and 6 to be fair, and scores of ≤ 4 to be low. Any discrepancies in the quality assessment were settled via negotiation.

Statistical analysis

Statistical analyses were conducted using Stata/SE (Statistics Data Analysis Special Edition) version 12.0 software (StataCorp LP, College Station, TX, USA). For dichotomous data, the relative risk and 95% confidence interval (CI) were used to represent the effect sizes, while the standard means difference (SMD) with 95% CI was used for continuous data. The I^2 test was used to assess statistical heterogeneity in the included studies, and $I^2 > 50\%$ and $p < 0.10$ represented substantial heterogeneity.^[32] In case of any heterogeneity, the sensitivity analysis, subgroup analysis, meta-regression, or the random-effects model were applied for clarification.^[33] The publication bias was evaluated with the following methods: the funnel plots, the Begg's or Egger's test,^[34] the trim-and-fill analysis, and the fail-safe number.^[35]

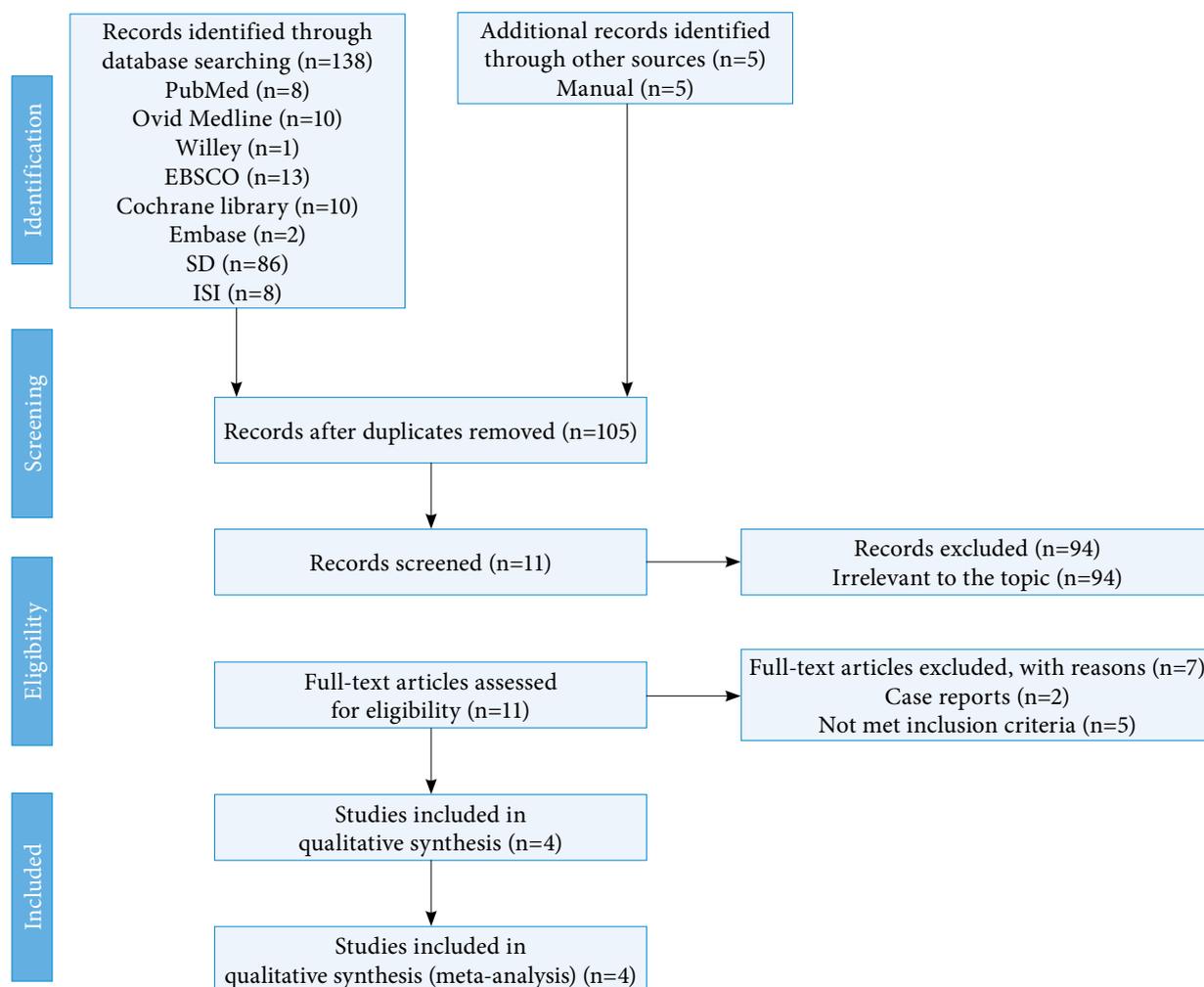


Figure 1. Search flowchart of the meta-analysis.

ID	Year	First author	1	2	3	4	5	6	7	8	9	10	Score	Eligibility criteria
1	2017	Areeudomwong et al. ^[1]	Y	Y	Y	N	N	Y	N	N	Y	Y	6	Y
13	2018	Areeudomwong et al. ^[1]	Y	Y	Y	N	N	Y	Y	N	Y	Y	7	Y
20	2006	Kofotolis et al. ^[20]	Y	N	Y	N	N	N	N	N	Y	Y	4	N
36	2014	Lee et al. ^[35]	Y	N	Y	N	N	N	Y	N	Y	Y	5	Y

1: Random allocation; 2: Concealed allocation; 3: Baseline similarity; 4: Blinding of subjects; 5: Blinding of therapists; 6: Blinding of assessors; 7: Measures of key outcomes from more than 85% of subjects; 8: Intention to treat analysis; 9: Between-group statistical comparisons; 10: Point measures and measures of variability.

RESULTS

Study selection

Comprehensive research recorded 143 references through electronic and manual searches. After excluding duplicates, screening titles and abstracts,

and assessing the full text in accordance with the study selection criteria, four studies^[1,13,20,36] reported between July 7, 2006, and October 9, 2018, were finally included in this study. The research flowchart is displayed in Figure 1 and detailed as supplementary information (SI) in Table 1.

TABLE 2
Heterogeneity tests, met-analyses and sensitivity analyses

Outcomes	No. of study	Eligible patients	Heterogeneity test	SMD	95% CI	<i>p</i>
PI all included	4	184	$p=0.237$ ($I^2=29.1\%$)	-0.835	-1.139, -0.531	<0.001
RMDQ all included	2	86	$p=0.085$ ($I^2=66.4\%$)	-1.765	-2.264, -0.888	<0.001
ODI all included	1	58	-	-0.893	-1.434, -0.352	0.001
HRQOL-P all included	1	42	-	1.817	1.092, 2.541	<0.001
HRQOL-M all included	1	42	-	-0.006	-0.611, 0.599	0.985

SMD: Standard means difference; CI: Confidence interval; PI: Pain intensity; RMDQ: Roland-Morris Disability Questionnaire; ODI: Oswestry Disability Index; HRQOL-P: Health-related quality of life-physical; HRQOL-M: Health-related quality of life-mental.

Quality assessment

The methodological quality of the included studies were assessed using the PEDro scale (<https://www.pedro.org.au/>). The quality scores of two studies could be extracted from the PEDro database, while the other two were assessed by the authors based on the PEDro criteria. The mean quality score was 5.5 ± 2.2 (range, 4 to 7). The quality evaluations were summarized in Table 1.

Study characteristics

Four studies with 184 patients (mean age: 37.8 ± 3.1 years; range, 35 to 50 years), 91 patients in the experimental group and 93 in the control group, were involved in this review. Three were conducted in Asia (two in Thailand and one in Korea), and one did not mention the study setting. The intervention used in the experimental group was PNF, and the control group interventions included sham PNF, routine

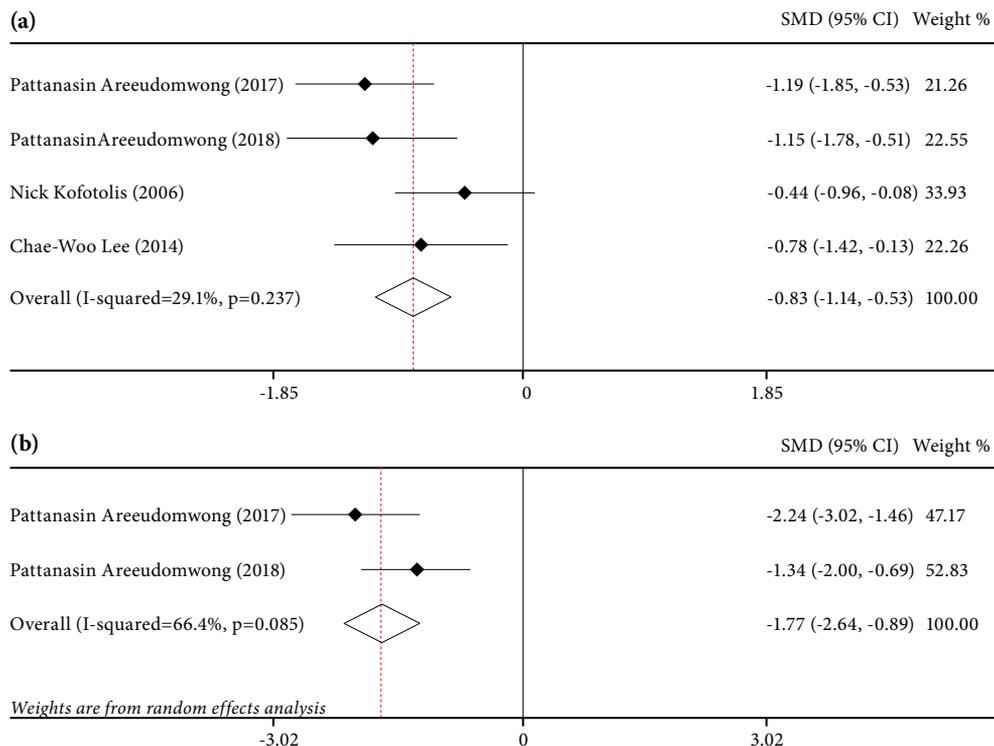


Figure 2. Forest plots of pain intensity and RMDQ.

RMDQ: Roland-Morris Disability Questionnaire.

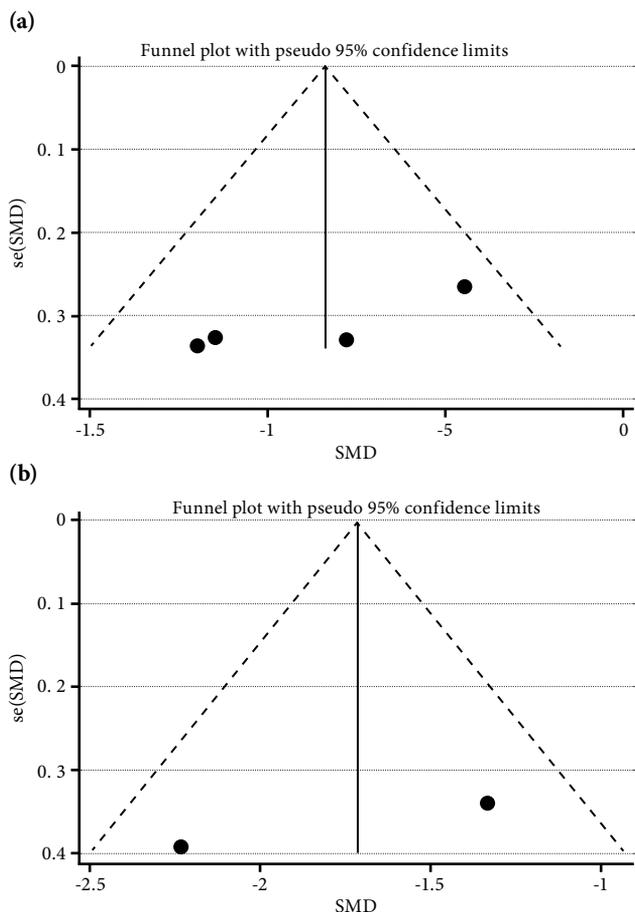


Figure 3. Funnel plots of pain intensity and RMDQ. SMD: Standard means difference; RMDQ: Roland-Morris Disability Questionnaire.

rehabilitation training, blank control, or education for patients with CLBP. The pain intensity data included Visual Analog Scale (VAS; two studies),^[37] numeric pain rating scale (NPRS; one study),^[38] and Borg back pain intensity scale (BBPS; one study).^[39] The IA data included the Roland Morris Disability Questionnaire (RMDQ)^[40] and the Oswestry Disability

Index (ODI).^[41] The HRQOL data consisted of physical (HRQOL-P) and mental (HRQOL-M) functions of quality of life.^[42,43] Table 2 demonstrates the detailed characteristics of the included studies.

Results synthesis

Effect size of pain intensity

The pain intensity data (four studies, 184 patients)^[1,13,20,36] were analyzed with a fixed-effects model and showed no significant heterogeneity ($I^2=29.1\%$, $p=0.237$). The pooled SMD and 95% CI: (-0.835 and (-1.139, -0.531), $p<0.001$) revealed that PNF relieved the pain in patients with CLBP compared to the control group, which was confirmed in the forest plots (Figure 2a). More information about meta-analysis was detailed as SI in Table 2. The sensitivity, subgroups, and meta-regression analyses could not be conducted due to the small number of included studies. For publication bias analysis,^[44] the funnel plots were visually symmetrical (Figure 3a), which indicated no obvious publication bias. The Begg’s and Egger’s tests also confirmed this ($p=0.308$; $p=0.105$; respectively). All details related to publication bias analysis were shown as SI in Table 3.

Effect size of RMDQ

The pooled RMDQ data (two studies, 154 patients)^[1,13] showed positive but heterogeneous results with a random model ($I^2=66.4\%$, $p=0.085$). The results showed that PNF improved individual activities in patients with CLBP (SMD: -1.765, 95% CI: -2.642 to -0.888, $p<0.001$, Figure 2b, SI Table 2). The visually symmetrical funnel plot (Figure 3b) and the Begg’s test ($p=1.000$, SI Table 3) suggested that no publication bias was observed.

Effect size of ODI

Oswestry Disability Index data (one study, 58 patients)^[20] was not pooled with the meta-analysis, and the positive SMD and 95% CI: (-0.893, -1.434 to -0.352,

TABLE 3 Publication bias analyses				
Outcomes	No. of study	Patients	Begg’s test	Egger’s test
PI	4	184	P = 0.308	P = 0.105
RMDQ	2	86	P = 1.000	-
ODI	1	58	-	-
HRQOL(P)	1	42	-	-
HRQOL(M)	1	42	-	-

PI: Pain intensity; RMDQ: Roland-Morris Disability Questionnaire; ODI: Oswestry Disability Index; HRQOL-P: Health-related quality of life-physical; HRQOL-M: Health-related quality of life-mental.

$p=0.001$) should be interpreted prudently in clinical settings (SI Table 2).

Effect size of HRQOL-P and HRQOL-M

The HRQOL data (one study, 42 patients)^[1] conveyed discrepant results. The HRQOL-P data yielded positive results (SMD: 1.817, 95% CI: 1.092 to 2.541, $p<0.001$), while the HRQOL-M data showed that PNF did not improve the psychological state in patients with CLBP (SMD: -0.006, 95% CI: -0.611 to 0.599, $p=0.985$, SI Table 2).

Safety assessments

No serious adverse events were reported in all four studies included.

DISCUSSION

In the present study, it was confirmed that PNF could relieve the pain intensity and improve individual activities and the physical function of the quality of life without any serious adverse events in middle-aged patients with CLBP by comparison with conventional medical care, rehabilitation, and sham PNF. The efficacy of PNF for CLBP was evaluated with pain intensity, RMDQ, ODI, HRQOL, and safety assessments.^[45-47] First, for the relief of pain intensity, the present study showed the positive results for PNF in CLBP without any heterogeneity and publication bias. Second, the results demonstrate that the scores of RMDQ and ODI were both significantly decreased after the PNF treatment, which verified the efficacy of PNF for the alleviation of disability in CLBP patients. Third, the study revealed that PNF improved only the physical function of HRQOL, although this was not meta-analyzed. Finally, the results of this study also suggest that the PNF is relatively safe as no adverse events were reported in any of the included studies. Compared with previous studies, our results are consistent with a recent narrative review,^[18] other two meta-analyses^[12,48] designed as PNF+Swiss ball versus PNF or PNF + dynamic soft tissue mobilization (DSTM) versus PNF, proving the value of PNF + Swiss ball or PNF+DSTM for patients with CLBP. Based on the present and previous studies, PNF could be recommended as a promising therapeutic modality for CLBP patients.

Proprioceptive neuromuscular facilitation can be applied as an adjunctive therapy with conventional care or as a standalone modality in recent clinical guidelines for low back pain.^[49,50] Based on the above results and discussion, it is suggested that the PNF therapy should be referred to patients with

CLBP. The frequency, intensity, time, and type of PNF were recommended as follows: (i) frequency and intensity, 15 sets/group, 30-60 sec rest/group, 3 groups/time, 3-5 times/week, 4-6 weeks; (ii) time: 30-45 min/time; (iii) type, the diagonal and spiral direction PNF.

There were some limitations in the present study. First, only four randomized controlled trials were included in the meta-analysis, and the sample size was small ($n=184$). Second, the efficacy of PNF for CLBP was assessed on short-term data (immediately after intervention) since the data related to the long-term follow-up were not reported in all included studies. Third, the age of the recruited patients ranged from 35 to 50 years; therefore, the effect of PNF on the young or aged patients with CLBP could not be confirmed. Lastly, there is substantial heterogeneity in the treatment duration, frequency, and intensity in the included studies. More rigorously designed and multi-center randomized control trials with a large sample size to evaluate the efficacy of PNF for various populations in CLBP are needed. The standardization of the PNF protocol should be given more attention based on the frequency, intensity, time, and type parameters. In addition, the long-term efficacy and adverse events of PNF for CLBP should be assessed in future RCTs.

In conclusion, this systematic review provided current evidence that PNF could relieve pain and improve individual activities without any serious adverse events in patients with CLBP; however, it should be cautiously recommended due to the small number of included randomized controlled trials.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Methodology, writing-review & editing, funding acquisition: L.L.X.; Writing-original draft, data curation, analysis: H.K.Y.; Data curation, analysis: Z.R.; Supervision, conceptualization: L.Z.Y.; Analysis, visualization: P.L.H.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

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