

Evaluation of dextrose prolotherapy versus extracorporeal shock wave therapy for pain relief and functional improvement in patients with knee osteoarthritis



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ABSTRACT

Background: Knee osteoarthritis (OA) remains a leading degenerative joint disease and a primary driver of chronic pain and disability among older adults. This condition is clinically defined by progressive cartilage degradation, joint stiffness, and a significant loss of functional mobility. Because standard conservative treatments often fail to provide adequate relief, there has been growing interest in regenerative approaches such as extracorporeal shock wave therapy (ESWT) and dextrose prolotherapy (DP). While their clinical use is increasing, direct comparative evidence regarding their relative effectiveness is still largely missing from some studies. This study aimed to evaluate the differences between ESWT and DP affect patients with knee OA in terms of functional improvement as measured by the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and pain reduction as measured by the Visual Analogue Scale (VAS).

Methods: This quasi-experimental study employed a pre-test–post-test randomised group design. Twenty patients with grade II–III knee OA who were not improving with traditional therapy were recruited and randomly assigned to two groups: ESWT (n=11) and DP (n=9). The interventions lasted for six weeks. Both before and after the intervention, the WOMAC and the VAS for pain were assessed as outcome measures. A statistical study was conducted to find differences both within and between groups.

Results: Both the ESWT and DP groups had statistically significant improvements in all metrics, including pain (VAS), WOMAC pain, stiffness, disability, and total scores ($p < 0.05$). However, there were no significant differences between the two groups for any of the evaluated outcomes ($p > 0.05$).

Conclusion: ESWT and DP were equally effective in reducing pain and improving functional outcomes in patients with knee OA. These findings indicate their role as a successful alternative therapy for people who don't receive enough relief from conventional medical therapies. Additional randomized controlled research are required to confirm these conclusions.

Keywords: dextrose prolotherapy, ESWT, knee osteoarthritis, regenerative therapy, WOMAC, VAS.

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INTRODUCTION

Some characteristic of knee osteoarthritis (OA) as a chronic, progressive, and degenerative joint condition such as osteophyte formation, synovial inflammation, subchondral bone remodelling, and destruction of cartilage are characteristics of knee osteoarthritis (OA).^{1,2} This condition leading to major cause of pain, disability, and a decline in older individuals' quality of life all across the world.³ The knee joint is the most often impacted area by OA due to its complex biomechanics and weight-bearing

function, which make it particularly vulnerable.⁴

Knee OA has a significant worldwide burden with raising prevalence rates according age. From population-based studies, prevalence rates in Asia range from 16 to 23 percent, affecting up to 80% of those over 75 and nearly 50% of adults over 60.^{5,6} According to estimates, between 10 and 14 percent of Indonesians suffer with OA, which is a serious public health issue.⁷ Genetics, obesity, repetitive mechanical stress, and occupational exposure are contributing concerns, especially in underdeveloped nations

where manual labour ergonomics are frequently ignored.⁸⁻¹⁰ The functional restrictions brought on by knee OA severely limit everyday tasks including crouching, mounting stairs, and getting out of a chair, which reduces independence and overall health-related quality of life.^{11,12}

A multimodal strategy combining pharmaceutical and non-pharmacological approaches is usually used to manage knee OA. Exercise, weight management, patient education, and bracing are highlighted as first-line non-pharmacological therapy in the 2019 American College of Rheumatology (ACR) guidelines.¹³

Pharmacological approaches that focus more on symptom management than disease modification include analgesics, intra-articular corticosteroids, and nonsteroidal anti-inflammatory medications (NSAIDs).¹⁴ Even though total knee arthroplasty (TKA) is still useful for end-stage conditions, it is not always accessible in low-resource environments, sometimes expensive, and carries certain surgical risks.¹⁵ Also, many patients in fall into the “treatment gap”, those for whom conservative therapy has failed but who are not yet candidates for TKA. Consequently, it is necessary to investigate alternate regenerative and minimally invasive therapies.

One possible non-invasive regenerative treatment for knee OA is extracorporeal shock wave therapy (ESWT). Focused acoustic waves are delivered to cause microtrauma, promote angiogenesis, and improve cartilage regeneration. By altering nociceptive pathways, it also produces analgesic effects.^{16–18} Clinical trials show notable pain reductions and enhanced functional outcomes, while preclinical research has shown benefits in subchondral bone remodelling and cartilage healing.^{19–22} Compared to surgical procedures, ESWT has the benefits of being non-invasive, reasonably safe, and cost-effective.²³

Another regenerating strategy is dextrose prolotherapy (DP), which involves injecting hypertonic dextrose solution intra-articularly or peri-articularly. The suggested method entails triggering the release of growth factors, inducing a localised inflammatory response, and then promoting collagen synthesis and tissue strengthening.^{24,25} According to clinical data, DP helps patients with knee OA increase their functional mobility, decrease chronic pain, and strengthen their joints.^{26,27} It is accessible in situations with minimal resources since it is quite safe, affordable, and may be done in an outpatient setting.²⁸

Although both ESWT and DP have demonstrated clinical benefits independently, head-to-head comparative evidence remains scarce. In Indonesia, access to specific therapies may be limited by cost or equipment availability, making a comparison between ESWT and the

DP regenerative option highly relevant to local clinical decision-making. Previous studies have largely evaluated their effects in isolation, leaving uncertainty regarding their relative efficacy in improving pain and functional outcomes in knee OA. While, the present study was conducted to compare the clinical effects of focused ESWT and hypertonic DP on pain reduction and functional improvement in patients with grade II–III knee OA. The Visual Analogue Scale (VAS) was used a thorough assessment as a consideration for measuring subjective pain severity and a major factor in OA patients’ decision to seek treatment. In addition, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) was used because of there is three crucial domains such as pain, joint stiffness, and physical function for disease-specific functional status. These tools were chosen because they have been proven to be reliable, are widely accepted in clinical research, and offer a comprehensive assessment of the patient’s capacity to carry out everyday tasks like walking and stair climbing, activities that are essential to rehabilitation. This study aimed to evaluate the differences between ESWT and DP affect patients with knee OA in terms of functional improvement as measured by the WOMAC and pain reduction as measured by the VAS.

METHODS

Research Design and Setting

This study was carried out at the Dr. Soetomo General Hospital’s Outpatient Rehabilitation Medicine Clinic in Surabaya, Indonesia from April to November 2024 by compared the therapeutic effects of DP and ESWT on pain severity and functional status in patients with OA of the knee using a quasi-experimental pre-test–post-test randomized group design.

Ethical Considerations

The study protocol was approved by the Institutional Review Board and Ethics Committee (Ethical Clearance Number: 0964/KEPK/IV/2024). Written informed consent was obtained from all participants prior to enrollment. All procedures complied with the ethical principles of human subject research and the Declaration of Helsinki.

Participants

Patients aged ≥ 40 years with a clinical and radiographic diagnosis of Kellgren–Lawrence grade II–III knee osteoarthritis and persistent knee pain despite at least four weeks of standard conservative rehabilitation were eligible for inclusion. Exclusion criteria included: history of knee surgery or intra-articular injection within the last three months; inflammatory or infectious arthritis; coagulopathy or anticoagulant therapy; severe neurological disorders affecting lower limb function; and contraindications to ESWT or injection therapy. Eligible participants were consecutively recruited and randomized into one of two intervention groups.

Randomization and Group Allocation

A total of 20 eligible participants were randomly allocated using a simple randomization method with computer generated sequence into: ESWT group ($n = 11$) and Dextrose prolotherapy group ($n = 9$). All participants continued receiving standard knee OA education and joint protection advice. Before the intervention, the subjects get baseline data by measuring VAS and WOMAC score by the author.

Intervention Protocols

Extracorporeal Shock Wave Therapy (ESWT)

Participants in the ESWT group received focused extracorporeal shock wave therapy once weekly for 6 consecutive weeks. ESWT was delivered to peri-articular knee structures and points of maximal tenderness, following standardized rehabilitation clinical protocols. Treatment intensity was administered within therapeutic parameters without local anesthesia. The dose protocol is low Energy Flux Density (EFD) ($0.08–0.28 \text{ mJ/mm}^2$), total number of shocks per session (2000 shocks at the affected knee), frequency start at 4 Hz increase up to 8 Hz in 6 weeks, with Richard Wolf piezoelectric Focus ESWT.

Dextrose Prolotherapy (DP)

The DP group received hypertonic dextrose injections once every 3 weeks, for a total of three sessions over 6 weeks. The solution was injected into targeted peri-

articular and intra-articular knee regions under aseptic conditions by experienced rehabilitation physicians. Injection sites and volumes followed established clinical prolotherapy protocols (DP 25% with 4 cc for intra-articular (suprapatellar recess) and 15% with 1cc each for peri-articular (MCL, LCL, patella tendon, pes anserine bursae, coronary ligament medial and lateral) with ultrasound guided)

Outcome Measures

Assessments were performed at baseline (pre-intervention) and after the six-week intervention period.

Primary outcomes included

The Visual Analogue Scale (VAS) is used to evaluate the intensity of pain (0–10). The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), which includes subscales for pain, stiffness, physical function, and overall score, is used to evaluate functional status. Every outcome tool has been verified and is frequently utilised in clinical research on knee OA. The author examined the VAS and WOMAC post-intervention results without knowing the type of interventions patients received.

Statistical Analysis

Data were analyzed using standard statistical software. Normality of continuous variables was assessed using the Shapiro–Wilk test. Within-group comparisons (pre- and post- intervention) were evaluated using paired t-tests or Wilcoxon signed-rank tests as appropriate. Between-group differences in outcome changes were analyzed with independent t-tests or Mann–Whitney U tests. A p -value < 0.05 was considered statistically significant.

RESULTS

A total of 20 patients with knee osteoarthritis who met the inclusion criteria were enrolled in this study and randomly assigned into two groups, these are ESWT group (11 participants) and DP (9 participants). Both groups demonstrated homogeneous baseline demographic and clinical characteristics, indicating comparability prior to intervention (Table 1).

Table 1. Normality test

Characteristic	Shapiro-Wilk
Age	0.131
Body weight	0.896
Body height	0.666
Body mass index	0.382
VAS Pre-Intervention	0.000
VAS Post-Intervention	0.001
Knee OA onset	0.001
Pain sub-scale WOMAC Pre-Intervention	0.106
Stiffness sub-scale WOMAC Pre-Intervention	0.004
Difficulty sub-scale WOMAC Pre-Intervention	0.421
Total score WOMAC Pre-Intervention	0.457
Pain sub-scale WOMAC Post-Intervention	0.333
Stiffness sub-scale WOMAC Post-Intervention	0.002
Difficulty sub-scale WOMAC Post-Intervention	0.234
Total score WOMAC Post-Intervention	0.211

Cm, centimetre; kg, kilogram; OA, osteoarthritis; VAS, visual analogue scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index

Analysis of the gender distribution showed a marked prevalence of female participants, representing 90% of the total study population. This finding is in line with some research that suggests hormonal swings and biomechanical variations in pelvic and knee alignment make women more vulnerable to degenerative joint disease.^{22–23} The ESWT and DP groups had mean ages of 53.91 and 52.33 years, respectively (Table 2). The overall mean BMI was 28.56 kg/m², placing them in the overweight to mildly obese range, which is recognized to be a mechanical risk factor for the accelerated deterioration of articular cartilage.^{23,24}

As seen by steady decrease in VAS and WOMAC ratings after the intervention period, both the ESWT group and the DP group showed statistically significant improvements in pain intensity and functional status. The ESWT group experienced a clinically significant decrease in pain, as evidenced by a decrease in the median VAS score from 5 at baseline to 2 after treatment also improvements in WOMAC subscale scores, such as a decrease in mean pain score from 3.36 to 1.18, a decrease in median stiffness score from 3 to 1, and an improvement in physical function, as indicated by a decrease in mean score from 8.09 to 3.73. The overall WOMAC score was significantly reduced from a mean of 14.27 to 5.64. The median VAS score decreased

from 5 to 2 in patients receiving DP, and the WOMAC assessment revealed significant decreases in mean pain, stiffness, and physical function scores from 4.11 to 1.78, 4.89 to 4.22, and 8.89 to 4.22, respectively. This findings in a decrease in the overall WOMAC score from a mean value of 16.89 prior to treatment to 7.22 following intervention. All observed changes within both treatment groups were statistically significant ($p < 0.05$), indicating that both ESWT and DP were associated with significant reductions in pain, stiffness, and functional limitations in patients with knee osteoarthritis who had previously shown inadequate improvement following standard rehabilitation therapy (Table 2).

There were no statistically significant variations in pain intensity or functional status, as indicated by changes in VAS and WOMAC ratings, between the ESWT and DP groups when post-intervention outcomes were compared. Statistical testing revealed that the magnitude of change in VAS scores did not differ substantially between the two groups ($p > 0.05$), indicating a comparable degree of pain reduction after intervention, even though both treatment techniques showed significant intragroup improvements. ESWT and DP both produced parallel improvements in pain, stiffness, and physical function, according to comparisons of WOMAC subscale ratings. These comparisons also revealed

Table 2. Characteristics of 20 participants of this study

Characteristic	Both groups N (%) or Mean±SD or Median (min-max) (n=20)	ESWT N (%) or Mean±SD or Median (min-max) (n=11)	DP N (%) or Mean±SD or Median (min-max) (n=9)	P-value
Gender				
Male	2 (10.0)	1 (50)	1 (50)	0.711 ^a
Female	18 (90.0)	10 (55.6)	18 (44.4)	
Age, years	53.20±4.53	53.91±5.10	52.33±3.84	0.455 ^b
Body weight, kg	69.80±13.50	67.36±13.66	72.78±13.47	0.387 ^b
Body height, cm	155.90±7.36	154.82±7.97	157.22±6.76	0.482 ^b
BMI, kg/m ²	28.56±4.19	27.89±3.98	29.38±4.53	0.445 ^b
OA anatomy location				
Unilateral	14 (70.0)	9 (64.3)	5 (35.7)	0.217 ^a
Bilateral	6 (30.0)	2 (33.3)	4 (66.7)	
Knee OA onset, months	12 (5-48)	12 (6-48)	12 (5-24)	0.843 ^c
Grade OA Unilateral				
II	15 (75.0)	10 (66.7)	5 (33.3)	0.098 ^a
III	5 (25.0)	1 (20.0)	4 (80.0)	
VAS Pre-Intervention	5 (4-6)	5 (4-5)	5 (4-6)	0.327 ^c
VAS Post-Intervention	2 (0-3)	2 (0-3)	2 (1-3)	0.422 ^c
WOMAC score Pre-Intervention				
Pain	3.7±1.55	3.36±1.56	4.11±1.53	0.299 ^b
Stiffness	4 (1-7)	3 (1-4)	4 (2-7)	0.153 ^c
Difficulty	8.45±3.56	8.09±4.11	8.89±2.93	0.631 ^b
WOMAC total score	15.45±5.49	14.27±5.83	16.89±4.98	0.302 ^b
WOMAC score Post-Intervention				
Pain	1.45±1.14	1.18±1.07	1.78±1.20	0.152 ^b
Stiffness	1 (0-2)	1 (0-2)	1 (0-2)	0.142 ^c
Difficulty	3.95±2.43	3.73±2.64	4.22±2.27	0.664 ^b
WOMAC total score	6.35±3.66	5.64±3.72	7.22±3.59	0.349 ^b

Cm, centimetre; DP, dextrose prolotherapy; ESWT, extracorporeal shock wave therapy; kg, kilogram; kg/cm², kilogram per metre squared; min-max, minimum-maximum; n, number of subject; OA, osteoarthritis; SD, standard deviation; VAS, visual analogue scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index

^a Fisher-Exact test; ^b Independent t-test; ^c Mann-Whitney test

no significant intergroup differences. The change in total WOMAC score further supported this finding, as the mean improvement observed in the ESWT group (8.64) was not statistically different from that observed in the DP group (9.67) ($p = 0.608$) (Table 3).

These findings suggest that ESWT and DP were equally effective during the study's short follow-up period in lowering pain and enhancing functional outcomes in patients with osteoarthritis in their knees who had not seen significant improvements from conventional rehabilitation therapy.

Table 3. Differences in functional status between knee osteoarthritis (OA) patients who received extracorporeal shock wave therapy (ESWT) compared to dextrose prolotherapy (DP)

Functional status after intervention	ESWT Mean±SD or Median (min-max) (n=11)	DP Mean±SD or Median (min-max) (n=9)	P-value
Change in VAS pain scale	3 (2-5)	3 (2-4)	0.205 ^b
Changes in WOMAC Pain	2.18±1.53	2.33±1.11	0.808 ^a
Changes in WOMAC Stiffness	2 (1-4)	3 (1-5)	0.325 ^b
Changes in WOMAC Difficulty	4.36±3.17	4.67±2.06	0.808 ^a
Change in total WOMAC score	8.64±4.63	9.67±4.06	0.608 ^a

min-max, minimum-maximum; n, number of subject; SD, standard deviation; VAS, visual analogue scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index

^a Independent t-test; ^b Mann-Whitney test

DISCUSSION

In patients with knee OA who had not shown noticeable improvement after standard rehabilitation therapy, this study showed that both DP and ESWT contributed to significant improvements in pain intensity and functional status. Both therapies offer clinically significant advantages in the short-term management of knee OA, as seen by the observed decreases in VAS scores and enhancements in WOMAC outcomes. This supports their use as regenerative or adjunctive therapeutic alternatives for patients who experience persistent symptoms.

Following therapy, there was a noticeable improvement in the DP group's overall functional status and a considerable reduction in the intensity of their pain. These results are in line with other systematic reviews and randomised controlled trials showing that DP helps individuals with knee OA feel less pain and have better joint function. The regeneration potential of this intervention was highlighted by certain studies that showed sustained improvements in WOMAC scores 52 weeks after DP when compared to placebo and at-home exercise routines.²¹ Comparing DP to intra-articular saline injections, Teymouri *et al.* discovered that DP produced better improvements in pain, functional limitation, and range of motion.²² A recent meta-analysis by Khateri *et al.* further confirmed that DP significantly reduces pain and stiffness for up to 20 weeks post-intervention, reinforcing the consistency of its clinical benefits across different study designs and populations.²³ Although the follow-up period in the present study was relatively short, the direction and magnitude of improvement align with the existing literature, suggesting that DP may exert early therapeutic effects that precede longer-term tissue remodeling.

DP has demonstrated competitive or advantageous results when compared to other widely utilised injectable treatments. DP offers functional gains that are in line with or better than those of hyaluronic acid (HA) and platelet-rich plasma (PRP), according to meta-analyses, especially when it comes to WOMAC scores.²⁴⁻²⁶ Long-term functional outcomes seem to be comparable between PRP and DP,

despite the fact that PRP may provide marginally better short-term pain relief, particularly during the first six months.^{27,28} Importantly, as compared to PRP and HA injections, DP has a far lower cost and a better safety profile, with fewer side effects recorded.²⁹⁻³¹ These features make DP a desirable and useful choice, especially in healthcare environments with constrained funding or where cost-effectiveness is a key factor.

According to recent research, the ESWT group also showed notable improvements in functional status and pain reductions, which is in line with the use of ESWT for knee OA. When compared to placebo or sham treatment, meta-analyses have demonstrated that ESWT significantly improves VAS and WOMAC ratings.³² According to Ko *et al.*, focused ESWT (f-ESWT) outperforms radial ESWT (r-ESWT), especially in patients with mild OA. This is probably because f-ESWT may send higher-energy acoustic waves to deeper joint structures, such as subchondral bone.³³ Focused ESWT was used in this trial, which may account for the notable improvements in function and discomfort. By accessing deeper subchondral bone, it became the best option for Grade II–III OA.^{34,34} Previous studies have demonstrated that focused ESWT can stimulate the release of growth factors such as vascular endothelial growth factor (VEGF) and bone morphogenetic protein-2 (BMP-2), as well as anti-inflammatory cytokines including interleukin-10 and transforming growth factor- β , contributing to cartilage regeneration and modulation of inflammatory processes.^{34,35} In contrast, radial ESWT primarily targets superficial soft tissues and periarticular structures and may be more suitable for patients with mild OA or predominant periarticular pain. In patients with mild-to-moderate OA, Zhao *et al.* found significant improvements in WOMAC and VAS ratings after radial ESWT; however, the strength and longevity of these effects were often less than those seen with targeted ESWT.³⁶ When compared to radial ESWT, targeted ESWT consistently produces larger and longer-lasting reductions in pain and impairment, especially in individuals with Kellgren–Lawrence grade

II–III OA.^{37,38} These findings support the preferential use of focused ESWT when deeper joint pathology and subchondral involvement are present.

There are very few direct comparisons between DP and ESWT in the global literature. Nonetheless, new data from regional research in Indonesia offers some first understanding of their relative efficacy. In patients with mild knee OA, Arfianti *et al.* found that both ESWT and DP significantly decreased VAS ratings, with little variation difference between treatment groups.³⁹ Similar pain reduction was seen by Fahmi *et al.* after ESWT and DP in patients who were not responding to conventional rehabilitation; however, ESWT seemed to have a quicker analgesic effect initiation.⁴⁰ These results align with the current study's findings, which showed no statistically significant differences between DP and ESWT in terms of functional improvement or pain reduction, indicating that both modalities provide similar short-term clinical effects.

Both therapies eventually affect comparable biological processes involved in the pathogenesis of knee OA, although having different starting mechanisms of action (biochemical stimulation for DP and mechanical energy transduction for ESWT). These include improving microcirculation, promoting tissue regeneration, reducing synovial inflammation, and regulating both central and peripheral pain.^{23,34,35} The identical clinical outcomes seen in both therapy groups, as seen by equivalent gains in VAS and WOMAC ratings, may be explained by this convergence of downstream effects. This result might be due to some theory such as the convergence theory that both focused ESWT and hypertonic dextrose (15–25%) target the same downstream pathways, such as the stimulation of growth factors like VEGF and BMP-2 or the modulation of synovial inflammation. Importantly, there is 6 weeks window and the differences might emerge at 6 months, as DP relies on collagen remodelling which takes longer than the immediate desensitization often seen with ESWT.^{23,34,35} Given that focused ESWT and DP demonstrated equivalent short-term clinical efficacy in this study, treatment selection should be individualized based on specific clinical objectives, patient

characteristics, and resource availability.⁷⁻¹⁰ Focussed ESWT provides a fully non-invasive regeneration option, clinicians may give it priority for patients who exhibit needle anxiety or a higher risk of localised infection.²⁷⁻³¹ In addition, when a quick onset of analgesia is needed to enable early participation in intense physical therapy and loading regimens, ESWT might be the best option. On the other hand, DP is still a very practical and affordable choice, especially in primary care or settings with low resources where access to specialised focused ESWT technology may be limited.³⁰⁻³⁵ Because the injection protocol enables the simultaneous targeted delivery of hypertonic solution to multiple anatomical structures, including intra-articular and peri-articular regions, DP is also beneficial for patients displaying multiple tender points or diffuse peri-articular symptoms.³¹⁻³³

This study has a number of limitations that should be noted. Conclusions on absolute treatment efficacy are limited by the lack of a placebo or standard-care control group, and the small sample size limits the statistical power to detect subtle differences between treatment groups. Furthermore, the comparatively short follow-up time might not adequately reflect the DP and ESWT's long-term regeneration benefits. To confirm these results and better define the best treatment indications, sequencing, and patient selection, future research with bigger sample numbers, longer follow-up periods, and multicenter designs is required.

CONCLUSION

For individuals with knee osteoarthritis who had not responded well to conventional rehabilitation, ESWT and DP as regenerative treatments were both successful in reducing pain and improving functional status. Both therapy groups showed notable short-term clinical benefits, as evidenced by the significant increases in VAS and WOMAC scores. Therefore, therapeutic goals, patient characteristics, available resources, and financial considerations can all be taken into account when choosing a treatment. When quick pain relief is required, ESWT might be useful, but DP provides a more affordable choice with a good safety profile.

ETHICAL CLEARANCE

Ethical approval was obtained from the Health Research Ethics Committee of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia (Ethical Clearance Number: 0964/KEPK/IV/2024)

CONFLICT OF INTEREST

None

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AUTHOR CONTRIBUTION

IMYP, NIH, AJAH, and LY were responsible for the conceptualization of the study, carried out the literature search, proceeded with the experimental procedures, analyzed the data, and prepared, edited, and reviewed the manuscript; NIH served as the guarantor for the integrity of the work.

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