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## Effect of percussion massage gun on hamstring flexibility in patients with knee osteoarthritis: A Randomized controlled trial

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### Abstract

**Background:** Decreased muscle flexibility and altered joint mechanics are connected to the onset and progression of osteoarthritis in the knee. The hamstring muscles tend to shorten and contract, which increases the tibiofemoral joint compressive force. Particularly for the hamstrings, stretches and percussive massage might help lessen the limitation of knee extension that is seen in patients with tibiofemoral osteoarthritis or patellofemoral pain syndrome. **Purpose:** to examine how utilizing a percussion massage gun affects people with knee osteoarthritis' hamstring flexibility, discomfort, range of motion, and function. **Methods:** 42 patients, ranging in age from 45 to 60 years, of both genders with mild to moderate knee OA were split into two groups of twenty-one patients each at random. Group A, or the control group, received standard physical therapy care involving strengthening and stretching the muscles in the lower limbs for four weeks, three workouts a week. Group B (the experimental group) received the same exercise as Group A in addition to a percussion massage gun on the hamstrings for five minutes, three sessions per week for four weeks. The sit-and Reach test was used to assess hamstring flexibility, the VAS for pain, active knee extension for knee extension ROM, and the WOMAC questionnaire to assess knee joint function. **Results:** There was a significant improvement ( $P < 0.05$ ) in hamstring flexibility, pain, ROM, and function in group B compared to group A. **Conclusions:** Percussion massage guns may have a significant effect on improving hamstring flexibility, pain, ROM, and function. This may benefit patients in improving their complaints, and this may benefit physiotherapists as well in improving their practice, as it is simple, easy, effortless, and more effective compared to stretching, especially in cases where knee extension is not recommended.

**Keywords:** Hamstrings flexibility, Knee osteoarthritis, Percussion massage, Strengthening exercises, WOMAC questionnaire

## Introduction

Osteoarthritis is regarded by the World Health Organization as a major public health concern. It is one of the main factors contributing to reduced function and a global decline in quality of life (QOL)<sup>1</sup>. Degenerative joint condition called osteoarthritis mainly affects the elderly. It is distinguished by subchondral sclerosis, enlargement of the bone along the edges (osteophytes), and degradation of the articular cartilage<sup>2</sup>.

In persons 50 years of age or older, around 65% of cases of knee discomfort are due to osteoarthritis (OA). This syndrome is linked to knee pain, decreased function, and tibiofemoral OA development. About 11% of adult patients with osteoarthritis in their knees require assistance with personal hygiene<sup>3</sup>.

There is a propensity for the hamstring muscles to shorten, and this shortening and tightening increases the patello-femoral compressive strain. This can eventually cause patello-femoral syndrome, which is frequently linked to osteoarthritis<sup>4</sup>.

According to Trudel, prolonged periods of immobility can cause atherogenic changes in the knee, which might result in the formation of a tightness. According to these authors, if a particular treatment plan is implemented to address the adaptive shortening of the surrounding muscles, healing from the tightness might be achievable<sup>5</sup>.

Other researchers have discovered that when walking and performing daily tasks, people who have osteoarthritis in their knees exhibit higher hamstring muscle activation<sup>6</sup>. Hamstring stretches may be particularly beneficial in minimizing the loss of knee extension in people who have osteoarthritis in their knees. Increases in joint range of motion have been shown in studies examining the effects of acute or single stretching sessions in various muscle group<sup>7</sup>.

Medication and several physiotherapy techniques, such as heat, massage, electrotherapy, and exercise, make up conservative treatment<sup>8</sup>. Exercise, physical therapy, losing weight, and wearing braces or heel wedges are among the physical modalities used to alleviate knee pain in people with osteoarthritis. For those suffering from osteoarthritis in their knees, exercise and weight loss are useful strategies for reducing discomfort and enhancing function, according to an evaluation of physical therapy interventions<sup>9</sup>.

A relatively recent method called "Percussion Therapy" applies percussive massage using a mechanical device, like a massage gun. Using a percussion massage gun releases tension and promotes flexibility while also by triggering a calming reaction and stimulating the Golgi tendon organ, it can enhance blood flow and the supply of nutrients to the tissue.

Furthermore, by utilizing pain gait theory, it lessens the impression of pain<sup>10</sup>.

The purpose of this study was to examine the workings of percussion massage guns affected the ROM, discomfort, and flexibility of the hamstrings in individuals with osteoarthritis of the knee.

## Methods

The aim of this study was to investigate the effect of using percussion massage gun on Hamstring flexibility, pain, ROM and Function in patients with knee osteoarthritis.

The Ethics Review Committee of Cairo University's Faculty of Physical Therapy gave its approval to this project. Egypt. registered in clinical trials with ID (NCT05988307). This study was conducted from April 2023 to September 2023 at the Outpatient Clinic of Faculty of Physical Therapy, Pharos University, Alexandria, Egypt.

## Study design

Pretest-post-test randomized control study.

## Participants

The sample size for this study was 42 patients divided randomly into two groups (n=21 in each group). Sample size calculation was based on power analysis done using G\* power software 3.1 program. the calculations were based on 1.06 effect size with an alpha level of 0.05, a desired power of 90%, two tailed unpaired test and 1:1 allocation ratio.

The sample was randomly divided into two groups A and B using opaque, sealed envelopes, each containing the name of one of the groups.

**Group A (conventional group):** went through a traditional physical therapy program including stretching, strengthening and neuromuscular rehabilitation exercises.

**Group B (Percussion massage group):** went through a traditional physical therapy program in addition to percussion massage gun.

Orthopedists, who were in charge of making the clinical diagnosis based on radiological testing, referred all of the patients. After inclusion in the study, all subjects signed a consent form, all personnel data, past medical history, were collected at the beginning of the study. Patients were assessed before and after four weeks (three sessions per week) of the treatment program

## Inclusive Criteria:

1. Age - 45 to 60 years patients of chronic knee OA.
2. Patients with BMI < 30 kg/m<sup>2</sup> (not being classified as obese)

3. Patients who are able to walk with painful knee OA without assistive devices.
4. Patients with knee pain intensity level at least  $>3$  cm on a 10 cm VAS scale in activities such as going up and downstairs, sitting and squatting.

#### **Exclusive criteria**

1. Radiated pain from low back pain.
2. Patients with no radiographic evidence of knee OA or with mild OA (grade I according to K/L classification) or with severe OA (grade IV according to K/L classification) as mild patients may not be confirmed by X-rays and severe patients may need surgeries or assistive device.
3. Loss of joint play in tibiofemoral and patellofemoral articulations.
4. Lower extremity fracture and surgery or trauma to the knee joint.
5. Neurological deficit or movement disorder related to lower limb.
6. Those who were athletes or who had been treated with physiotherapy or medications during the previous 6 weeks.
7. Those who could not apply vibration and percussion stimuli.
8. Those who had varicose veins.

#### **Instrumentations**

##### **Instrumentations for assessment**

1. 100 cm Ruler
2. Visual analogue scale (10 cm) for pain intensity assessment
3. A digital goniometer that measures the knee joint's range of motion in degrees of an angle.
4. An osteoarthritis index developed by Western Ontario and McMaster Universities for the Arab community to evaluate knee function, The WOMAC index in Arabic is a valid and reliable tool for assessing the degree of knee OA.
5. Body mass index, weight, and height on a universal scale. ( $BMI = \text{weight (kg)} / [\text{height (m)}]^2$ ).

##### **Instruments for Treatment**

1. TheraBand for resistance, Sand bags.
2. Percussion Massage gun. gun (brand: phoenix, Model A2, country of manufacturing: China)

##### **Procedures for assessment**

Every patient had evaluations both prior to and following treatment.

##### **For Measuring Hamstring Muscle Flexibility**

The participants in each group were evaluated for flexibility using the sit-and-reach test. The lower limbs' feet, without shoes on, had the flexibility box positioned so that it touches the bottoms of their feet. The subjects were measured their hips while sitting on

a mat with their arms outstretched. The zero meters of a 100-cm adjustable meter ruler was placed at the tip of the right middle finger, in the middle of the box, between the two large toes<sup>11</sup>.

The participants were instructed to extend their backs and move their fingers as far as they could along the table to a new position. This position was held for five seconds, during which time the middle finger's tip was measured using a ruler to determine flexibility. Better performance was indicated by higher scores; the test was administered twice, with the average being kept. As the subjects of the experiment undergo the flexibility test, they were asked to rate their degree of knee pain on a VAS scale<sup>11</sup>.

Previous research has confirmed the validity of the sit and reach test ( $r=0.46-0.67$ ) for hamstring flexibility estimation<sup>12</sup>, and the reliability estimate is strong ( $0.96 < R < 0.99$ )<sup>13</sup>.



Figure (1): starting and ending position of sit and reach test.

##### **For Measuring Pain Intensity Level**

The pain that patients reported experiencing during activities of daily living was assessed using a visual analog scale (VAS)<sup>14</sup>.

##### **For measuring Knee extension ROM:**

Every group underwent the active knee extension test, and the findings were recorded on a goniometer in angle degrees. It was instructed for the participants to face the wooden frame while lying supine on the table. The leg under examination was bent till the thigh comes into contact with the wooden frame, once it reaches a 90-degree angle with the table. A second

examiner completely extended and stabilized the opposite limb in a neutral rotation. An electronic goniometer was positioned across the lateral femoral condyle while maintaining the foot in a neutral posture and the knee extended at a 90° angle. One arm was positioned parallel to the thigh, extending towards the greater trochanter, while the other arm was placed parallel to the leg, extending towards the lateral malleolus. The participants were instructed to straighten their knees until they felt strong resistance, without any kind of pre-warm-up exercises. The next step in taking a goniometric reading was to maintain this posture for two or three seconds<sup>15</sup>.

### ***Knee joint function using the WOMAC questionnaire Arabic version***

It was correctly completed just before treatment begins. The patient was instructed to complete the Arabic-language printed questionnaire in a quiet area. After being given the questionnaire subscales, the patient was requested to complete the 17-item physical function subscale, the Subscale measuring pain (5 items) and subscale measuring stiffness (2 items). Every item was rated from 0 (nothing), 1 (slight), 2 (moderate), 3 (extremely), and 4 (severe). All conversations took place in Arabic<sup>16</sup>. The elements for each of the three subscales are added up to produce the overall WOMAC score. Higher WOMAC ratings (between 0 and 96) correspond to worse pain, stiffness, and functional impairments<sup>17</sup>.

### ***Rehabilitation protocol:***

The two groups received conventional physical therapy program of 12 sessions, over four weeks.

**Group A (conventional group):** Over the course of 12 treatment sessions—three sessions each week—patients in group A underwent typical lower limb strengthening and stretching exercises, including resistance exercises for the quadriceps. Multiple angle isometric seated quadriceps knee extension exercises (30°, 60°, and 90°) were performed for three repetitions and three sets using TheraBand 10s for each angle. Three sets of ten repetitions of straight leg raising with ankle weight, three sets of ten repeats of ankle planter flexion with resistance using TheraBand, three sets of thirty seconds of hamstring stretching, and three sets of ten repetitions of hip abduction and adduction with weights (side laying) using ankle weights<sup>18</sup>.

**Group B (percussion massage group):** A traditional physical treatment regimen combined with percussive massage using a massage gun that pulses 40 times per second for five minutes each session<sup>19</sup>.

There are four distinct head attachments for the massage gun. The normal ball attachment was utilized for this investigation. Both tiny and large muscle groups can be targeted with this attachment. This attachment was the best fit because it addressed the hamstrings<sup>20</sup>. After applying the percussion therapy gun to the subject's leg for five minutes, moving the massage gun's head from proximal to distal, all three of the hamstring complex's muscles experienced myofascial release. A portion of the hamstring complex, such as trigger points, that the participant felt tight or sensitive received an additional 30 seconds of percussion therapy. This made the myofascial release more successful. Overall, the use of this tool improved blood flow and relaxed muscles, which helped the participant's range of motion and produced myofascial release<sup>21</sup>. The patient's affected side was where the therapist stood. The patient is on the treatment table, lying down prone, while using a massage gun .<sup>10</sup> (Fig.2).



**Figure (2):** Application of percussion massage gun

### ***Statistical analysis***

Data were expressed as mean± SD. Unpaired t-test and chi square were used to compare between subjects' characteristics of the two groups. Shapiro-Wilk and Kolmogorov-smirnov tests were used for testing normality of data distribution. MANOVA was performed to compare within and between groups' effects for all measured variables; hamstring flexibility, pain intensity, knee extension ROM and knee functional disability. Statistical package for the social sciences computer program (version 20 for Windows; SPSS Inc., Chicago, Illinois, USA) was used for data analysis. P less than or equal to 0.05 was considered significant.

### ***Results:***

#### ***Demographic data of subject***

Out of 42 patients who were enrolled in the study, 21 were randomly assigned to the control group (A) and given a standard physical therapy regimen; 21 were assigned to the experimental group (B) and given

a standard physical therapy regimen plus percussion massage gun. As shown in **table 1**

**Table (1): Demographic data of subjects of both groups**

Demographic data	Group A	Group B	t-value	p-value
Age (years)	49.6±4.4	48.6±3.8	0.753	0.456
BMI (g/m <sup>2</sup> )	26.2±1.6	26.3±1.7	0.237	0.814
Sex	N (%)	N (%)		
Males	7 (33.3%)	5 (23.8%)	$\chi^2=0.465$	0.734
Females	14 (66.7%)	16 (76.2%)		

$\chi^2$ : chi square, p- value: significane

**Normality test:**

The normality assumption, variance homogeneity, and presence of extreme scores were checked in the data. With  $p>0.05$ , the Shapiro-Wilk and Kolmogorov-Smirnov tests proved that all of the measured variables were normally distributed.

all of the measured variables were normally distributed.

**Effect of treatment on all variables included in the analysis:**

To examine how the therapy affected the assessed variables, MANOVA was used.

The primary effects of time ( $p=0.001$ ) and treatment ( $p = 0.004$ ) were statistically significant, and the interaction effect of treatment times time was also statistically significant ( $p=0.001$ ) **Table 2**.

**Table 2: MANOVA table for the effect of treatment on the measured variables**

Interaction effect (treatment * time)	p- value	$\eta^2$
$F = 121.2$	$p = 0.001$	0.929
<b>Effect of time</b>		
$F = 749$	$p = 0.001$	0.988
<b>Effect of treatment</b>		
$F = 4.62$	$p = 0.004$	0.334

F value: Mixed MANOVA F value, p value: Probability value,  $\eta^2$ : partial eta square

**The impact of percussion massage gun on Hamstring flexibility**

**Within group comparison**

Group A: The mean  $\pm$  SD of sit and reach test pre- and post-treatment of group A was  $-14.6 \pm 4.3$  and  $-10.2 \pm 3.2$  respectively. Patients in Group A had a 30% reduction in sit-and-reach test scores after treatment compared to before treatment ( $p = 0.001$ ).

Group B: The mean  $\pm$  SD of sit and reach test pre- and post-treatment of group B was  $-15.9 \pm 4.4$  and  $-5.7 \pm 1.9$  respectively. Both the pre- and post-treatment scores on the sit-and-reach test were significantly lower (64% lower,  $p = 0.003$ ) in group B. (**Table 3**).

**Between groups comparison**

The mean scores of the sit and reach tests did not differ statistically significantly between the two groups prior to treatment ( $p=0.341$ ), There was a statistically significant difference between the groups after treatment ( $p=0.001$ ), which favored group B. (**Table 3**).

**The impact of percussion massage gun on pain intensity:**

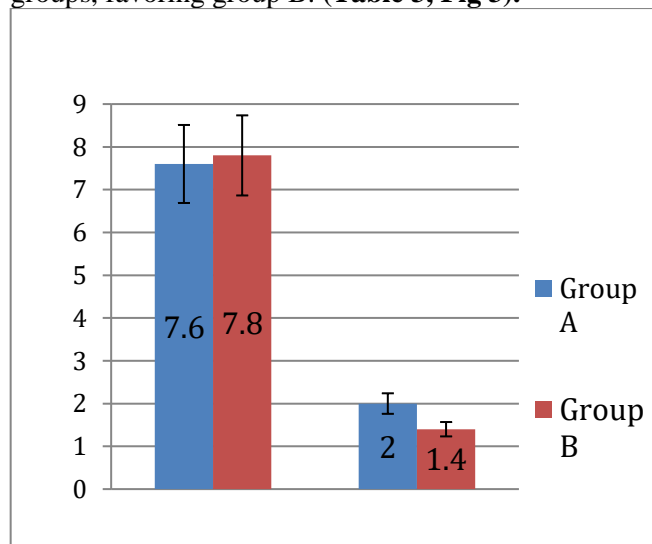
**Within group comparison**

**Group A:** Group A measured an average  $\pm$  SD of  $7.6 \pm 1.1$  cm of pain before treatment and  $2 \pm 0.3$  cm of discomfort after treatment. By 73.7% ( $p = 0.001$ ), the level of pain in group A was much lower after therapy than it had been before.

**Group B:** Before therapy, Group B had an average pain level of  $7.8 \pm 0.7$  cm, and after treatment, it was  $1.4 \pm 0.4$  cm. After therapy, Group B reported significantly less pain (82% reduction compared to pre-treatment levels;  $p = 0.001$ ). (**Table 3**).

**Between groups comparison**

Before treatment, there was no statistically significant difference in the mean pain levels between the two groups ( $p=0.513$ ), but after treatment, there was a significant difference ( $p=0.001$ ) between the two groups, favoring group B. (**Table 3, Fig 3**).



**Figure (3):** Mean values of pain pre and post treatment between groups

**The impact of percussion massage gun on knee extension ROM:**

**Within group comparison**

**Group A:** The knee extension of group A was  $141.6 \pm 7.2$  degrees before therapy and  $164.7 \pm 2.9$  degrees after treatment. The knee extension of group A increased by 16.3% after therapy compared to before treatment ( $p = 0.001$ ).

**Group B:** The knee extension of group B was  $145 \pm 7.6$  degrees before therapy and  $174.2 \pm 1.4$  degrees after treatment, as measured by the mean  $\pm$  SD. Results showed that after treatment, knee extension in group B was 20.1% higher than pre-treatment ( $p = 0.001$ ). (Table 3).

**Between groups comparison**

The mean values of knee extension did not differ statistically significantly between the two groups prior to treatment ( $p=0.141$ ), while group B benefited from a statistically significant difference between the groups following treatment ( $p= 0.001$ ). (Table 3, Fig 4).

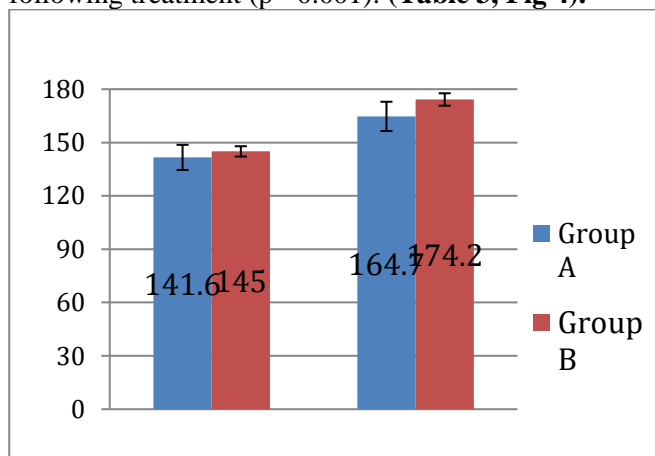


Figure (4): Mean values of knee extension pre and post treatment between groups

**The impact of percussion massage gun on knee function disability:**

**Within group comparison**

**Group A:** The mean  $\pm$  SD of WOMAC pre- and post-treatment of group A was  $55.9 \pm 5.9$  and  $49.5 \pm$

4.9 respectively. There was a statistically significant decrease in WOMAC in group A post-treatment compared with that of pre-treatment by 11.4% ( $p = 0.001$ ).

**Group B:** The mean  $\pm$  SD of WOMAC pre- and post-treatment of group B was  $56 \pm 5.4$  and  $39.3 \pm 3.8$  respectively. There was a statistically significant decrease in WOMAC in group B post-treatment compared with that of pre-treatment by 29.8% ( $p = 0.001$ ) (Table 3).

**Between groups comparison**

The mean WOMAC values did not differ statistically significantly between the two groups before treatment ( $p= 0.978$ ), whereas group B benefited from a statistically significant difference between the groups after treatment ( $p= 0.001$ ). (Table 3, Fig 5).

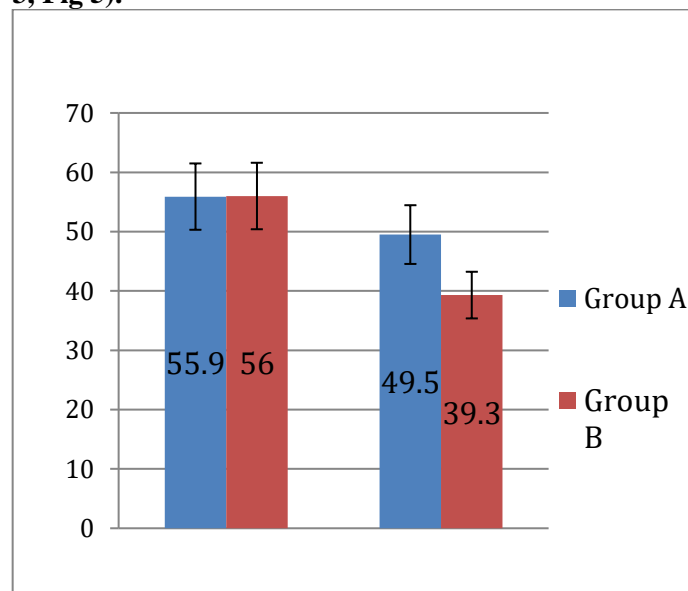


Figure (5): Mean values of WOMAC pre and post treatment between groups

Table (3): Mean  $\pm$ SD of measured variables pre and post treatment of both groups.

Measured variables	Group A Mean $\pm$ SD	Group B Mean $\pm$ SD	f-value	P-value	$\eta^2$
<b>Hamstring flexibility</b>					
Pre-treatment	$-14.6 \pm 4.3$	$-15.9 \pm 4.4$	0.927	0.341	0.023
Post-treatment	$-10.2 \pm 3.2$	$-5.7 \pm 1.9$	29.473	0.001*	0.424
% of change	30%	64%			
P-value	0.001*	0.001*			
<b>Pain (cm)</b>					
Pre-treatment	$7.6 \pm 1.1$	$7.8 \pm 0.7$	0.435	0.513	0.011
Post-treatment	$2 \pm 0.3$	$1.4 \pm 0.4$	18.653	0.001*	0.318
% of change	73.7%	82%			
P-value	0.001*	0.001*			
<b>Knee extension (degrees)</b>					
Pre-treatment	$141.6 \pm 7.2$	$145 \pm 7.6$	2.255	0.141	0.053

Post-treatment	164.7 ± 2.9	174.2 ± 1.4	181.324	0.001*	0.819
% of change	16.3%	20.1%			
P-value	0.001*	0.001*			
<b>WOMAC</b>					
Pre-treatment	55.9 ± 5.9	56 ± 5.4	0.001	0.978	0.001
Post-treatment	49.5 ± 4.9	39.3 ± 3.8	55.832	0.001*	0.583
% of change	11.4%	29.8%			
P-value	0.001*	0.001*			

SD: standard deviation, \*: significant,  $\eta^2$ : Partial eta square

## Discussion

This study looked at how utilizing a percussion massage gun affected people with knee osteoarthritis' hamstring flexibility, discomfort, range of motion, and function.

In this study, 42 individuals of both genders who were diagnosed by orthopedic surgeons as having mild to moderate osteoarthritis (OA) and were recommended for physical therapy treatment were included.

All patients were assessed prior and after treatment the included patients were assessed to determine hamstring flexibility, pain, ROM and physical function using WOMAC questionnaire. Then received Four weeks of traditional strength training program (group A) and four weeks of traditional program with percussion massage (group B).

### For hamstrings flexibility:

The findings of this study about the impact of using a percussion massage gun on increasing hamstring flexibility were in line with the findings of a previous study. It examined the impact of physical therapy (PT) on the flexibility of the hamstrings in a prone adult patient, aged 25. Physical therapy was administered for five minutes every day for a week to the hamstring muscles in the abdomen, utilizing a large ball head attachment to move up and down. Additionally, the sit and reach test and the 90-90 test were performed. The assessment of hamstring flexibility was conducted using these methods, and the results showed an increase in flexibility<sup>22</sup>.

Additionally, it was approved by Godemeche, N., who looked into how 25 adult male volunteers' lower limb and lower spine flexibility was changed by physical therapy. After 16 minutes of ROM while lying prone, the gastrocnemius, hamstrings, gluteus, and lumbar muscles were massaged unilaterally for 2 minutes each. Significant improvements were observed in the sit and reach test after physical therapy ( $p < .05$ )<sup>23</sup>.

### For pain:

According to the current study's results, group B experienced a much greater improvement ( $P < 0.05$ ) in

pain reduction than group A. These outcomes demonstrated the percussion massage gun's efficaciousness in reducing pain.

The findings of this investigation on the impact of utilizing percussion massage gun on reducing pain aligned with the findings of Moral Piñero, M.'s study. Examine the differences in pain and flexibility between Myofascial Induction plus Percussion Therapy and Massage plus Manual Vibration. Myofascial plus PT treatments lasted 30 minutes, and ROM was assessed using a goniometer and the VAS for pain. Significant differences in active knee extension and hamstring extensibility ( $p < .001$ ) were found between the PT group (mean = 9.60°) and the alternative treatment group (mean = 5.20°). Pain: There were significant differences in the VAS ( $p = .017$ ), with the PT group's mean score being 3.80 and the other group's score being 2.80<sup>24</sup>.

### For knee extension ROM:

The current study's findings demonstrated that group B's knee extension significantly improved ( $P < 0.05$ ) compared to group A's. These outcomes demonstrated how well applying the percussion massage gun can enhance range of motion for the knee extension.

The findings of this study on the impact of utilizing a percussion massage gun on enhancing knee extension range of motion were consistent with the findings of Hernandez, F. A.'s study, which evaluated the impact of physical therapy on lower body muscular passive range of motion and sports performance. Apply bilateral Percussion therapy on the following muscle groups: calves, planter, quadriceps, hamstrings, and the gluteus maximus and medius. 30s with a standard head attachment for each muscle group. Muscle bellies at a constant, acceptable pressure are followed by PT from the proximal to the distal regions. Knee ROM was measured using the 90-90 test; the results showed a significant increase in ROM in the hip ( $p < .001$ ) and ankle ( $p < .001$ ) following physical therapy. ROM for knee extension also rose ( $p = .001$ )<sup>25</sup>.

To reinforce the current findings even more, Sams, L. carried out a thorough evaluation of the literature to determine how percussion therapy affected adult populations' musculoskeletal function and pain

perception. The study involved the use of massage guns to administer percussion therapy directly to the muscle belly or tendon, and compared the results to those of no treatment, placebo, and alternative treatments. Thirteen trials that satisfied the inclusion criteria suggest that, whether compared to other treatments, placebos, or no treatment at all, physical therapy administered with massage guns can enhance an acute response in terms of flexibility and pain sensations<sup>26</sup>.

Furthermore, Martin, J.'s systematic review. An analysis of percussion massage gun devices with an emphasis on lower limb mobility as a rehabilitation tool. This literature evaluation made use of thirty-nine included studies. As a result, range of motion was so enhanced, and the consequences of delayed onset muscle soreness were minimized. Using portable percussion massagers like the Hypervolt Thera gun or other massage guns. They discovered that range of motion can be sharply increased with just one massage gun application<sup>20</sup>.

#### Limitations:

- 1-The study was not concluded on a large scale and study sample was considerably less.
- 2-The study was limited to short time, for further studies longer time with periodical follow up should be included.

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- 3-The study was not included measurement of muscle performance.

#### Conclusions

The study results confirmed the effective role of percussion massage gun on the hamstring flexibility, pain, ROM and function in people who have OA in their knees.

#### Authors' contributions

The authors have determined that all individuals indicated as authors are eligible for authorship. The content and similarity index of the paper are the responsibility of all authors who have critically evaluated and approved the final version.

#### Availability of data and materials

The collected and analyzed data during the study are available upon reasonable request and following institutional approval from the corresponding author.

#### Conflict of interest

This article has no potential for a conflict of interest.



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