Comparación entre la terapia de ondas de choque extracorpóreas y la proloterapia con dextrosa sobre el rendimiento del músculo cuádriceps en la osteoartritis de rodilla

Comparison between extracorporeal shockwave therapy and dextrose prolotherapy on quadriceps muscle performance in knee osteoarthritis

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Abstract

Introduction: The Quadriceps Femoris muscle group frequently exhibits weakness in individuals diagnosed with knee Osteoarthritis (OA). This weakness arises from muscle atrophy and mechanisms such as arthrogenic muscle inhibition. Emerging therapies such as hypertonic Dextrose Prolotherapy (DP) and Extracorporeal Shockwave Therapy (ESWT) offer promising intervention for knee OA, focusing on pain relief and functional improvement. This study aims to evaluate and compare the effects between ESWT and DP on pain, quadriceps femoris muscle thickness and the Vastus Medial Oblique (VMO) electromyography (EMG) activity in knee OA patients. Methods: Eighteen subjects with grade 2-3 unilateral knee OA (Kellgren-Lawrence) randomized into ESWT and DP group. The ESWT group received six sessions of focused-ESWT therapy, with 1-week interval. The dextrose prolotherapy *(DP)* group received three-injection regime with 3-weeks interval between injections. The VAS score, Quadriceps Femoris muscle thickness measured by musculoskeletal ultrasound, and VMO EMG activity recorded by surface EMG (sEMG) were measured before and after the interventions.
Results: There were significant improvement of VAS score in both DP group ($p = 0.007$) and ESWT group ($p = 0.006$). The Quadriceps Femoris muscle thickness showed no significant improvement in both groups ($p > 0.05$), while VMO sEMG activity showed improvement of VMOmax in ESWT group ($p < 0.001$), and VMOavg in both groups ($p = 0.012$ and $p = 0.001$).
Conclusion: Both ESWT and DP improved pain and VMO EMG activity in knee OA patients, with comparable results between the two interventions. No significant changes of quadriceps femoris muscle thickness was found in both groups after the interventions.

Keywords

Dextrose prolotherapy (dp); extracorporeal shockwave therapy (eswt); osteoarthritis; quadriceps muscle; vastus medial oblique (vmo); good health; well-being.

Resumen

Introducción: El grupo muscular cuádriceps femoral presenta frecuentemente debilidad en individuos diagnosticados con osteoartritis de rodilla (OA). Esta debilidad surge de la atrofia muscular y de mecanismos como la inhibición muscular artrogénica. Las terapias emergentes como la proloterapia hipertónica con dextrosa (PD) y la terapia de ondas de choque extracorpóreas (TOCE) ofrecen una intervención prometedora para la OA de rodilla, centrándose en el alivio del dolor y la mejora funcional. Este estudio tiene como objetivo evaluar y comparar los efectos entre la PD y la TCE sobre el dolor, el grosor del músculo cuádriceps femoral y la actividad electromiográfica (EMG) del oblicuo medial vasto (VMO) en pacientes con OA de rodilla. Métodos: Dieciocho sujetos con artrosis unilateral de rodilla de grado 2-3 (Kellgren-Lawrence) asignados aleatoriamente a los grupos ESWT y DP. El grupo ESWT recibió seis sesiones de terapia ESWT focalizada, con un intervalo de 1 semana. El grupo de proloterapia con dextrosa (DP) recibió un régimen de tres inyecciones con un intervalo de 3 semanas entre ellas. La puntuación VAS, el grosor del músculo cuádriceps femoral medido por ecografía musculoesquelética y la actividad EMG del VMO registrada por EMG de superficie (sEMG) se midieron antes y después de las intervenciones.
Resultados: Hubo una mejora significativa de la puntuación VAS tanto en el grupo DP (p = 0,007) como en el grupo ESWT ($p = 0{,}006$). El grosor del músculo cuádriceps femoral no mostró una mejora significativa en ambos grupos ($p > 0{,}05$), mientras que la actividad sEMG del VMO mostró una mejora del VMOmax en el grupo ESWT ($p < 0{,}001$) y del VMOavg en ambos grupos (p = 0,012 y p = 0,001).
Conclusión: Tanto la ESWT como la DP mejoraron el dolor y la actividad electromiográfica del músculo VMO en pacientes con artrosis de rodilla, con resultados comparables entre las dos intervenciones. No se encontraron cambios significativos en el grosor del músculo cuádriceps femoral en ambos grupos después de las intervenciones.

Palabras clave

Proloterapia con dextrosa (DP); terapia de ondas de choque extracorpóreas (ESWT); osteoartritis; Músculo cuádriceps; Vasto oblicuo medial (VMO); buena salud; bienestar.

Introduction

Knee osteoarthritis (OA) is a chronic degenerative joint disease characterized by the deterioration of articular cartilage, subchondral bone remodeling, and synovitis. This condition frequently results in pain, stiffness, and reduced mobility, with significant limitations in activities such as walking and climbing stairs, particularly in the elderly population (Geng et al., 2023; Hsu & Siwiec, 2023). It is positively associated with obesity in older people with the Body Mass Index cut-off point of 29.78 kg/m^2 in elderly women is relevant indicator of increased risk (Ferrari et al., 2024).

The Quadriceps Femoris muscle group, essential for knee stability and leg extension, is often weakened in individuals with knee OA. This weakness arises from muscle atrophy and mechanisms such as arthrogenic muscle inhibition (AMI), a neural feedback alteration due to joint pathology (Lewek et al., 2004; David A Rice et al., 2011). Compared to healthy people, muscle thickness of the Vastus Medial (VM) were significantly decreased in mild knee OA and disuse atrophy may occur first in the VM muscle (Chen et al., 2023). Assessing quadriceps femoris muscle thickness and muscle electrical activity, especially the Vastus Medial Oblique (VMO) is clinically valuable for understanding knee OA-related functional deficits and for guiding rehabilitation strategies (David A Rice et al., 2011).

There are various methods for measuring and evaluating the contractile and biomechanical components the VMO. The electrical and mechanical activity of muscles can be monitored and recorded as maximum voluntary isometric contraction (MVIC) using surface electromyography (sEMG). It is a non-invasive examination that can be used to determine quadriceps muscle function activity (Linderman et al., 2023). Musculoskeletal ultrasonography (USG), measured muscle thickness, may also provide important information about muscle function. Study by Gellhorn et al (2018) showed that muscle thickness of the quadriceps correlates with pain and patient's function in adults with symptomatic knee OA (Gellhorn et al., 2018). It is thought that quadriceps muscle thickness can be increased by reduction of pain experienced by patients, especially during activity, thus may lead to increased participation in functional activities (Bozan & Erhan, 2023).

Based on the American college of rheumatology (ACR) Guideline for osteoarthritis (OA), only exercise, lifestyle modification, orthosis, knee brace, oral non-steroidal anti-inflammatory drugs (NSAID), topical NSAID, and intra-articular steroid are strongly recommended for treatment of OA (Kolasinski et al., 2020). However, those treatment modalities do not resolve the underlying cause of OA. Regenerative therapy is an alternative method proposed for OA, due to its capability to aid tissue regeneration, enhance clinical manifestations, and repair damaged tissue structures, which are pathological conditions in OA. Emerging therapies such as hypertonic Dextrose Prolotherapy (DP) and Extracorporeal Shockwave Therapy (ESWT) offer promising interventions for knee OA, focusing on pain relief and functional improvement (Uysal et al., 2020; Waluyo et al., 2023; Yildiz Mursit et al., 2023). Prolotherapy involves injecting hypertonic dextrose into ligaments, tendons, or joint spaces to stimulate healing mechanisms such as fibroblast proliferation, collagen synthesis, and enhanced ligament thickness. It is an invasive treatment to facilitate regeneration that will improve joint stability as well as reduce pain (Abdel-Fattah et al., 2024; Rabago et al., 2010; Sit et al., 2016). As a non-invasive treatment, ESWT delivers focused acoustic waves to musculoskeletal tissues, promoting mechano-transduction, angiogenesis, and tissue regeneration while alleviating inflammation and pain (Ma et al., 2020; Wuerfel et al., 2022).

Understanding the differential impact of prolotherapy and ESWT on quadriceps muscle function is critical, given its central role in knee stability and mobility. Research examining alterations in quadriceps activation predominantly depends on participant motivation. Evidence suggests that declines in quadriceps strength and activation may, to some extent, result from an unconscious modification of voluntary effort, possibly due to concerns about joint damage or pain associated with arthritis (David Andrew Rice & McNair, 2010). Prolotherapy has shown promise in promoting tissue repair and enhancing ligament and cartilage structure, while ESWT is known to facilitate cellular regeneration and pain modulation (Soliman et al., 2016; Wuerfel et al., 2022). ESWT can enhance gait parameters, including cadence and walking speed, in knee OA patients by modulating mechanoreceptor activity, promoting subchondral bone regeneration, and reducing pain through mechano-transduction pathways (Randita et al., 2023).

Although both therapies demonstrate efficacy in reducing pain and improving function, their comparative effects on structural and functional quadriceps femoris properties, such as muscle thickness measured by musculoskeletal ultrasound and VMO muscle electrical activity recorded with electromyography (EMG), remain unexplored (Ma et al., 2020; Sit et al., 2016). This study aims to evaluate and compare the efficacy between a non-invasive intervention (ESWT) and an invasive intervention (dextrose prolotherapy) on quadriceps femoris muscle thickness and the VMO EMG activity in knee OA patients. The findings are anticipated to guide evidence-based, individualized rehabilitation strategies for improving functional outcomes in this population.

Method

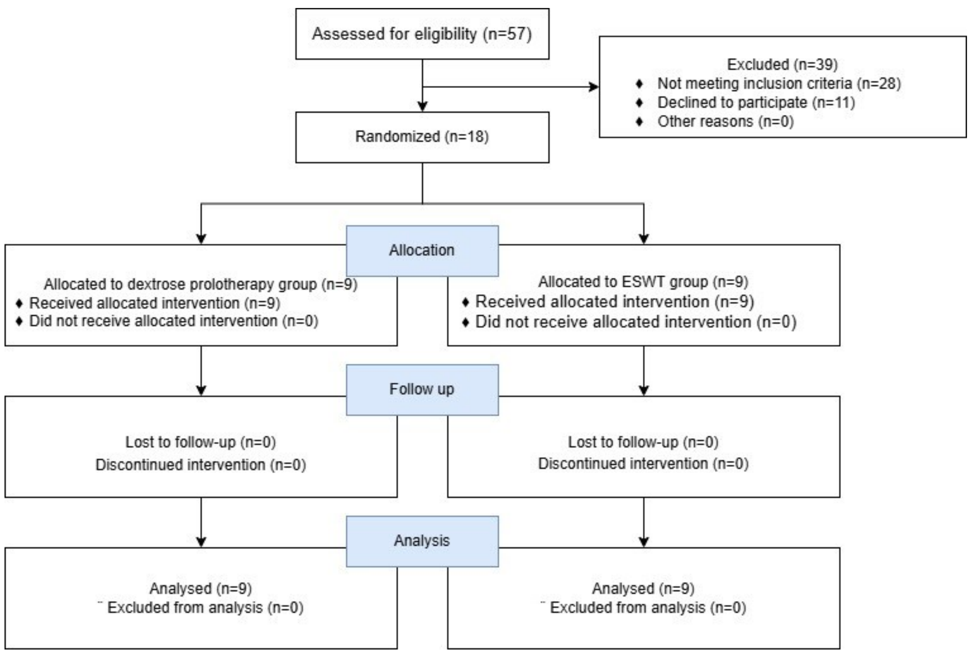
We carried out a prospective comparative study at the rehabilitation outpatient clinic of Dr. Soetomo General Academic Hospital in Surabaya, Indonesia. The ethical approval was obtained from The Ethical Committee of Dr. Soetomo General Academic Hospital Surabaya, Indonesia (No 0964/KEPK/IV/2024). Written informed consent obtained from participants before the study.

Participants

Participants were included in the study if they were adults aged 40-59 years who have been diagnosed with unilateral knee osteoarthritis, graded as Kellgren-Lawrence (KL) 2-3 based on radiological examination, had underwent standard rehabilitation program for one month period, able to walk independently (with or without assistive device). We excluded participants if they had any of the following conditions : had knee injections or dextrose prolotherapy in the past year, had ESWT therapy in the past year, local knee infections, acute arthritis, rupture of knee tendons or ligaments, malignancy, clotting disorders, currently on antithrombotic medication, pregnant women, autoimmune diseases, uncontrolled type 2 diabetes mellitus, immunocompromised, history of trauma to the lower limbs, deformities or restricted range of motion in the lower limbs, had neuromuscular diseases, obesity, and pain with Visual Analog Scale (VAS) > 6. The sample size was determined based on pilot study data from Randita (2023), using β = 0.20 and α = 0.05. (Randita et al., 2023).

Eligible participants were randomly assigned to either the dextrose prolotherapy (DP) group or the ESWT group. A consecutive sampling method was employed until the required number of participants was achieved. The study design flowchart is presented in Figure 1.

Figure 1. Flowchart of the Study



Procedure

The dextrose prolotherapy (DP) group received regiment of three-injection. The interval between injections were 3 weeks (Sert et al., 2020). The concentration of dextrose for intra-articular injections were 25% (4 ml), and for extra-articular injections were 15% (1 ml at each site target). The extra-articular injections were administered to the medial collateral ligament, lateral collateral ligament, pes anserine attachment, tibial tuberosity, coronary ligaments, and patellar tendon. The injection was performed under Ultrasonography (USG) guided, by physiatrist trained for Interventional Pain Management.

The ESWT group received six sessions of ESWT therapy, with 1-week interval (International Society for Medical Shockwave Treatment, 2023; Randita et al., 2023). We used focused-ESWT Piezo Shockwave2 (Elvation®, Germany) for treatment with energy settings of F10/G4, intensity of 0.27 mJ/mm^2, frequency of 4 Hz, and a total of 2000 shocks per session. Patients were placed in a supine position with the affected knee flexed 60°–90° in order to expose the joint cartilage during treatment. The physician located the pain area as the focus region that will receive a greater therapeutic effect by palpating the anatomical landmarks around the knee joint (the medial and lateral), and avoiding the main nerves and blood vessels area. Both groups receive education on knee joint conservation for daily activities.

The outcome measurements were quadriceps femoris muscle thickness measured with musculoskeletal ultrasound, and the Vastus Medial Oblique (VMO) EMG activity recorded by a surface EMG (sEMG) biofeedback unit. The measurement was evaluated before and one week after the interventions.

Sonographic examination of the quadriceps muscle thickness was performed by a physiatrist trained in musculoskeletal ultrasonography. The examination was performed using high-resolution ultrasonography General Electric type LOGIQ P6, with a 11 MHz linear array transducer. Muscle thickness was defined as the distance between the bone-muscle interface and the adipose-muscle interface. Measurements were taken from the most superficial edge of the bright line representing the bone-muscular cortex interface to the most superficial edge of the bright line marking the boundary between the outer fascial layer of the muscle and subcutaneous adipose tissue. Three images were captured at each location, and the average value was used for data analysis (Abe et al., 2014).

Quadriceps femoris electrical activity were measured using a 2-channel device (Myomed 932 sEMG Biofeedback Unit, Enraf Nonius, The Netherlands). Skin adhesive surface electrodes were used to record muscle activity. Gel-based electrodes were applied following the SENIAM (Surface Electromyography for Non-Invasive Assessment of Muscles) guidelines to measure muscle electrical activity (Hermens et al., 1999). Active and reference electrodes were positioned to capture the electrical activity of the vastus medialis oblique (VMO) muscle. The active electrode was placed 4 cm superiorly, while the reference electrode was positioned 3 cm medially from the superomedial border of the patella. Additionally, a ground electrode was affixed to the ipsilateral leg, 2–3 cm below the patella. The electrical activity of the VMO was recorded using surface electromyography (sEMG) during maximum voluntary isometric contraction (MVIC) of the quadriceps, performed three times with one-minute intervals. The average of these three trials was used to determine the VMO maximal (VMOmax) and VMO average (VMOavg) values.

Data analysis

Statistical Analysis were calculated using SPSS IBM 26th edition (MacOS version). The change in scores within each group was assessed using the Wilcoxon Signed-Rank Test for paired samples. Paired t test used to analyze the difference between two groups. Statistical significance defined as $p < 0.05$. Analysis of Covariance was conducted to look at important covariates.

Results

The study included 18 subjects (Table 1) that met the inclusion criteria. Baseline comparison of age, sex, Body Mass Index (BMI), Visual Analogue Scale (VAS), quadriceps femoris muscle thickness, and electrical activity (sEMG) of the VMO muscle (VMOmax and VMOavg) showed no between-group differences. Grade of OA severity (KL) showed significant between-group differences.

Table 1. Clinical Characteristics of the DP Group and ESWT Group

Characteristics	DP group (n=9) Mean ± SD	ESWT group (n=9) Mean ± SD	p*
Age (year)	52.33 ± 3.84	55.11 ± 3.10	0.110[a]
BMI (kg/m²)	27.12 ± 3.66	29.38 ± 4.53	0.263[a]
Sex			
Female	8	8	0.765[c]
Male	1	1	
Grade of KL			
Grade 2	5	9	0.041[c*]
Grade 3	4	0	
VAS	5.11 ± 0.60	4.88 ± 0.33	0.331[d]
Quadriceps femoris muscle thickness (cm)			
Short Axis	2.24 ± 0.85	2.59 ± 0.61	0.680[a]
Long Axis	2.39 ± 0.83	2.61 ± 0.61	0.310[a]
VMO sEMG activity (μV)			
VMO Max	71.75 ± 28.67	137.57 ± 102.42	0.085[d]
VMO Average	35.14 ± 12.53	62.68 ± 44.88	0.085[d]

a) Independent t-test; b) Chi-square test; c) Fisher exact test; d) Mann-Whitney test; *Statistically significant at $p < 0.05$

Table 2 showed significant difference in VAS score in both DP group and ESWT group before and after intervention (p = 0.007 and p = 0.006). The Quadriceps Femoris muscle thickness showed no significant improvement in both groups (p > 0.05). The VMO sEMG activity showed improvement in both DP group and ESWT group. The VMO max improved in ESWT group (p = < 0.001), but not in DP group (p = 0.366). The VMO average improved in both groups (p = 0.012 and p = 0.001).

Table 2. Inter group changes difference of Quadriceps Femoris Muscle Thickness, and VMO sEMG activity, pre and post intervention

Parameter	Pre & post intervention (n=18)					
	DP Group Pre (n=9)	DP Group Post (n=9)	p*	ESWT Group Pre (n=9)	ESWT Group Post (n=9)	p*
VAS	5.11 ± 0.60	2.00 ± 0.70	0.007[a*]	4.88 ± 0.33	2.00 ± 0.86	0.006[a*]
Quadriceps Femoris muscle thickness (cm)						
Short Axis	2.24 ± 0.85	2.15 ± 0.54	0.067[b]	2.59 ± 0.61	2.71 ± 0.48	0.437[b]
Long Axis	2.39 ± 0.83	2.15 ± 0.63	0.067[b]	2.60 ± 0.60	2.78 ± 0.50	0.090[b]
VMO sEMG activity (μV)						
VMO Max	71.75 ± 28.67	103.82 ± 63.50	0.366[b]	137.57 ± 102.42	122.24 ± 82.77	< 0.001[b*]
VMO Average	35.14 ± 12.53	42.76 ± 28.36	0.012[b*]	62.68 ± 44.88	59.42 ± 35.32	0.001[b*]

Values are mean ± standard deviation (S.D.); *Statistically significant at $p < 0.05$; a) Wilcoxon signed rank test; b) Paired t-test

Table 3 showed no significant difference in changes of VAS score, Quadriceps Femoris muscles thickness and VMO sEMG activity between DP group and ESWT group before and after intervention (p > 0.05).

Table 3. Between group changes difference of Quadriceps Femoris Muscle Thickness, and VMO sEMG activity, pre and post intervention

Parameter	Pre & post intervention (n=18)		
	DP group (n=9)	ESWT group (n=9)	p*
Changes of Quadriceps Femoris muscle thickness (cm)			
Short Axis	0.09 ± 0.54	-0.12 ± 0.48	0.600[a]
Long Axis	0.23 ± 0.63	-0.18 ± 0.51	0.310[a]
Changes of VMO *s*EMG activity (μV)			
VMO max	32.11 ± 60.16	-15.22 ± 35.70	0.059[a]
VMO average	7.56 ± 19.93	-3.33 ± 19.24	0.256[a]
Change of VAS	3.11 ± 0.78	2.89 ± 0.92	0.416[b]

Values are mean ± standard deviation (S.D.); *Statistically significant at $p < 0.05$; a) Independent t-test

Table 4 presents ANCOVA results assessing the effects of OA grade (2 vs. 3) and pre-intervention measures on quadriceps muscle thickness (short and long axis) and maximum VMO contraction. For short axis thickness, OA grade had no significant effect (p = 0.490), while pre-intervention thickness significantly influenced post-intervention values (p = 0.020). In the long axis, OA grade remained non-significant (p = 0.960), with pre-intervention thickness showing borderline significance (p = 0.050). In the VMO contraction analysis, OA grade (p = 0.360) and pre-intervention VAS (p = 0.850) were not significant predictors. However, pre-intervention VMO contraction strongly influenced post-intervention values (p < 0.001), suggesting baseline muscle activity is a key determinant of post-intervention outcomes.

Table 4. ANCOVA results assessing the effects of OA grade and pre-intervention measures on quadriceps muscle thickness and maximum VMO contraction

Measure	Covariate	dF	Mean Square	F-value	*p**
Short Axis Quadriceps Thickness	OA Grade (2 vs 3)	1	0.12	0.53	0.490
	Pre-Intervention Thickness	1	2	8.85	0.020*
Long Axis Quadriceps Thickness	OA Grade (2 vs 3)	1	0.0008	0.003	0.960
	Pre-Intervention Thickness	1	1.68	5.78	0.050
Max VMO Contraction	OA Grade (2 vs 3)	1	2403	0.88	0.360
	Pre-Intervention VAS	1	103	0.04	0.850
	Pre-Intervention VMO	1	48450	17.75	< 0.001*

*Statistically significant at $p < 0.05$

Discussion

Studies of ESWT and dextrose prolotherapy as a regenerative medicine-based treatment on knee OA mostly investigated clinical outcomes, not the muscle performance. Muscle is the power and control of joint activity, a link that cannot be ignored in the development of knee OA (Chen et al., 2023). This is one of the few studies to report comparison between Extracorporeal Shockwave Therapy (ESWT) and dextrose prolotherapy on muscle performance in knee OA patients. The results demonstrated that both groups achieved successful outcomes, as measured by lower VAS scores and increased in VMO activity. The quadriceps muscle thickness did not change after interventions in both groups. When the two groups were compared, we found no significant differences. This means that both treatments were comparable and showed equal effectiveness.

The significant improvement of pain observed in our study after ESWT intervention supported that ESWT is effective to reduce pain in knee OA. Pain is one of the major factors that prevent functional activity. The therapeutic effectiveness and safety profile of ESWT to reduce pain and promote regeneration in knee OA have been widely studied (Avendaño-Coy et al., 2020; Ma et al., 2020). We did not find any adverse effect in our study. The current proposed action mechanisms of ESWT are focused on the generation of low-grade inflammation, Facilitate bone healing, stimulate the formation of new blood vessels and tissue renewal, and potentially suppress the activity of pain-transmitting sensory receptors (Randita et al., 2023). We applied focused ESWT with intensity of medium energy flux densities (0.25 - 0.27 mJ/mm^2). According to systematic review study by Avendaño-Coy (2020), medium energy flux densities exerted greater effect to pain and function than low or high densities in mild and moderate knee OA. The study concluded that ESWT was considered as “moderate” recommendation level (according to GRADE) to reduce pain levels and improve functional abilities in those affected by knee osteoarthritis. (Avendaño-Coy et al., 2020).

Most studies were in accordance to our result that report positive effects of dextrose prolotherapy in knee OA. The main effects were on its pain relief and regenerative effect (Waluyo et al., 2023). The current understanding suggests that the injected solution mimics the body’s natural healing process by initiating a localized inflammatory response, which in turn releases growth factors and promotes collagen deposition. This process, mediated by cytokine-induced chemo-modulation, facilitates the proliferation of new connective tissue, enhances joint stability, and alleviates pain and dysfunction (DeChellis & Cortazzo, 2011). Combining hypertonic dextrose prolotherapy with conventional physiotherapy has demonstrated superior outcomes in reducing pain levels and improve functional abilities (Yildiz Mursit et al., 2023). It is also considered as low-cost therapy and widely-available in the clinical setting (Wee et al., 2021). However, the non-invasive and a low complication rate of ESWT could make it more interesting compared to more invasive treatment such as injection of dextrose prolotherapy for pain management in knee OA (Ma et al., 2020).

We measured the VMO sEMG activity as an evaluation of muscle performance in this study. A study by Chen et al (2023) concluded that the VM in bilateral knee OA patients may show muscle degeneration earlier (Chen et al., 2023). Our study showed that in the ESWT group, both the VMOmax and VMOavg showed significant improvement after 6 sessions of intervention with one-week interval. Significant weakness of the quadriceps muscles, particularly the VMO, is a common finding in individuals with knee osteoarthritis (OA). This weakness results partly from muscle atrophy and partly from persistent neural inhibition, which hinders full activation of the quadriceps. This phenomenon, known as arthrogenic muscle inhibition (AMI), is associated with joint swelling, inflammation, pain, laxity, and structural damage (David Andrew Rice & McNair, 2010). Besides reducing pain as shown in this study, ESWT had protective effects to subchondral bone layer, especially on the medio-tibial part of the knee joint. This will make the VMO able to contract efficiently providing good knee stability for functional activity (Randita et al., 2023). Other proposed mechanism underlying the improvement of VMO sEMG activity in our study were also due to the circulatory effects of increased blood and lymph flow after ESWT that may enhance muscle function and increase range of motion.

In the dextrose prolotherapy group, only the VMOavg, but not the VMOmax, showed significant improvement after three-injection regime with three-weeks interval. This result showed comparable effect with ESWT on muscle performance. Dextrose is believed to supply essential nutrients for repairing damaged cells, exert a direct influence on peripheral nerves, and enhance the strength of ligaments and tendons through the formation of fibrous tissue (Distel & Best, 2011; Rhatomy et al., 2020). Yildiz et al (2023) studied functional measurements with isokinetic dynamometer for extensor knee strength as the outcome measurement after dextrose prolotherapy injection compared to conventional physiotherapy. They concluded that the dextrose prolotherapy group had greater improvements in pain and functionality including knee muscles strength (Yildiz Mursit et al., 2023). When normal human cells are exposed to hypertonic dextrose, they begin to synthesize growth factors, including platelet-derived growth factor, transforming growth factor-beta, epidermal growth factor, basic fibroblast growth factor, and insulin-like growth factor (Reeves et al., 2008). These growth factors stimulate fibroblasts to produce precursors of mature collagen (DeChellis & Cortazzo, 2011). Furthermore, a mild chondrogenic effect of dextrose has been observed through arthroscopy and biomarker analysis (Topol et al., 2016; Waluyo et al., 2021). The combined effect of regenerative in the soft tissue surrounding the knee joint (periarticular) and pain relief could result in improved muscle performance of the quadriceps in our study.

The presence of knee OA is known to reduce isometric knee strength and this will worsen with disease severity. Many factors affect the strength of quadriceps muscle, one of them is muscle size. Muscle thickness is often associated with joint stability and function (Bozan & Erhan, 2023). Our study showed that the quadriceps femoris muscle thickness did not show improvement after interventions, both in the dextrose prolotherapy group as well as in the ESWT group. Between-group comparison also showed no significant difference. This is in accordance with study by Chopp-Hurley et al (2020) that concluded muscle thickness of the quadriceps was not related to any OA clinical severity outcomes. Other study showed that there was a significant relationship between quadriceps muscle thickness and knee OA stages and pain scores (Bozan & Erhan, 2023). We included participants who already underwent standard rehabilitation program for one month period. They also received education on knee joint conservation for daily activities. In order to increase the quadriceps muscle thickness, exercise focusing in muscle strengthening for at least 6 weeks are needed for knee OA patients (Abdelstar, 2024). This could be the reason why muscle thickness was not improved in our study.

Our study had several limitations. First, the present study did not monitor whether participants consistently followed the prescribed home-based exercise program, that could affect muscle performance and overall outcomes. Secondly, we included only patients with moderate OA (KL grade 2-3), but not the mild and severe OA (KL grade 1 and 4). Future studies should consider employing a more homogeneous distribution of participants across the different grades of knee osteoarthritis, ideally including all four Kellgren-Lawrence grades with a more balanced representation in both intervention groups. This approach would enhance the comparability between groups and allow for more accurate interpretation of treatment effects across varying severities of the condition. Additionally, extending the follow-up period to a minimum of 12 weeks is recommended to capture longer-term outcomes and provide a more objective assessment of intervention efficacy. Monitoring adherence to prescribed exercise programs is crucial to evaluate their influence on therapeutic outcomes. Exploring the potential synergistic benefits of combining ESWT and DP with conventional rehabilitation or pharmacological treatments is also recommended. Finally, mechanistic studies investigating the biological pathways influenced by these interventions could offer valuable insights for optimizing treatment protocols.

Conclusions

Both ESWT and DP improve pain scale and VMO activity in knee OA patient with comparable result between two interventions. However, no significant changes of quadriceps muscle thickness found in both ESWT and DP after intervention. The choice of which regenerative treatment (non-invasive or invasive) depends on physiatrist's clinical judgment and patient-care setting.

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