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Review article

Effectiveness of myofascial therapy on hemophilic arthropathy: A systematic review and meta-analysis of clinical trials

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ABSTRACT

Background: Recurrent hemarthrosis is one of the major complications affecting joint functions, and causing chronic pain in hemophilia patients.
Objective: To summarize the existing evidence of the effects of myofascial therapy (MFT) on joint status, joint pain, and hemarthrosis in hemophilic arthropathy.
Methods: This systematic review and meta-analysis was done according to PRISMA checklist. Finally, four clinical trials included and were pooled using STATA 13. Standardized mean difference (SMD) considered as the effect size.
Results: All patients in the case group received 3 interventions of MFT over a 3-week period and were evaluated for 1–5 months. Joint pain with and without load was significantly decreased after three weeks in the intervention group compared to controls (SMD: -0.61, 95% CI: -1.02, -0.21 and 0.58, 95% CI: -0.88, -0.28 respectively). Also, joint status significantly improved three weeks later in patients with MFT compared to controls. (SMD: -0.49, 95% CI: -0.79, -0.19) and this improvement remained until the end of the follow-up period (SMD: -0.54, 95% CI: -0.84, -0.24).
Conclusion: This meta-analysis showed that MFT can be an effective intervention improving the joint status and decreasing pain perception in patients with hemophilic arthropathy. Consequently, it can play an important role in achieving higher functionality and quality of life in these patients. However, due to the small number of studies and other limitations, further well-designed trials and updated meta-analysis are needed for more accurate results and interpretation.

1. Introduction

Hemophilia is a coagulopathy inherited recessively through X-chromosome, which leads to deficiency or dysfunction of clotting proteins including factor VIII and IX. There are two major types of hemophilia, namely hemophilia A or factor VIII deficiency and hemophilia B or factor IX deficiency [1]. The severity of disease in hemophilia is determined by the plasma level of factor VIII or IX activity, the severe is defined as factor level <1% of normal, the moderate 1–5%, and the mild form is demonstrated as factor level >5% and <40% [2].

The clinical manifestation of hemophilia A and B are generally similar [3]. The risk of hemorrhage depends on the severity of coagulation factor deficiency and patients' age. It can be manifested as intracranial and extra cranial hemorrhage in neonates [4], significant bleeding after circumcision [4], spontaneous muscle hemorrhage or hematoma, and intra articular bleeding [3]. Recurrent joint bleeding causes chronic inflammation of synovial tissue, progressive tissue destruction, join-surface erosions, and finally hemophilic arthropathy [5]. The ankle, knee, hip, and elbow are the most common involved joints [5]. Joint deformity is the late stage of hemophilic arthropathy affecting the joint functions, and causing chronic pain [6]. There are two major approaches of treatment in hemophilia: replacement therapy (prophylaxis) which is the administration of the deficient factor adequately to prevent bleeding and on demand treatment which means infusion of the deficient factor at the time bleeding occurred [7]. The most important complication of replacement therapy is development of inhibitors which are alloantibodies against

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the infused factors [8]. This process finally causes frequent episodes of bleeding that are difficult to control with lower response to concentrated factors [8]. In addition to factor replacement, conventional management including rest, ice, compression, and limb elevation can be helpful for joint bleeding [9]. There are different physiotherapy techniques including joint traction, kinesiotherapy, massage, and joint mobilization are branches of physical medicine that increase muscle movement and strength, induce joint healing, and improve joint condition. They also can be used for reducing the frequency of joint pain in different conditions that causes joint pain [10, 11]. Myofascial Therapy (MFT) or myofascial release is a widely applicable type of manual therapy aiming to promote the joint movement by promoting the re-orientation of facial collagen fibers [12]. It basically involves sustained mild pressure applied to fascia through direct and indirect methods. In the direct technique, the practitioner applies specific tools that produce a force of a few kilograms on the considered fascia. The indirect method, on the other hand, encompasses a gentle stretch with a few grams of force [13]. Myofascial release can improve arterial function as a cause of enhancement of vascular endothelial function by increasing plasma concentration of nitric oxide [14, 15]. Also, MFT can modulate the activity of autonomic nervous system and in long term, it can increase the joint flexibility and range of motion [14].

Up to now, several studies have been performed to determine the safety and effectiveness of MFT in joint heath score and joint pain in patients with hemophilia. However, there has been no systematic approach or meta-analysis on the evaluation of MFT effects. Therefore, the present meta-analysis aims to summarize the existing evidence on the effects of fascial therapy on hemarthrosis, joint status, and joint pain in patients with hemophilia.

2. Methods

This systematic review and meta-analysis was done according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist [16] and was registered in the International.

Prospective Register of Systematic Reviews (PRSPERO) with the confirmed code: CRD42022301703. The study protocol was also approved by the Ethical Committee of Shiraz University of Medical Sciences (Ethics code: IR. SUMS.REC.1400.797).

2.1. Search strategy

Searched databases: A systematic search was done by two independent authors (SH and MH-B) in December 2021. The searched databases included Web of Science (ISI), Scopus, PubMed, Cochrane Library, and Physiotherapy Evidence Database (PEDro). A combination of the following MeSH terms and keywords was used to conduct comprehensive literature searches: for population: ("Hemophilia A″ OR "Hemophilia B″ OR "Hemophilia" OR "Christmas Disease" OR "Factor VIII Deficiency" OR "Factor IX Deficiency"); for intervention: ("Myofascial Therapy" OR "Musculoskeletal Manipulation*" OR "Fascial therapy*" OR "Manual therapy*" OR "Physiotherapy" OR "Physical therapy*" OR "Manipulation Therapy*" OR "Manipulative Therapy*" OR "Active Release Technique" OR "Myofascial Release Techniques"). Moreover, the reference lists of the relevant articles and previously performed reviews were manually checked for additional pertinent studies.

Inclusion and exclusion criteria: The eligible studies were required to meet certain criteria including 1- being conducted on human subjects, 2- being conducted on patients with hemophilic arthropathy (elbows, knees, or ankles), 3- reporting the effects of fascial therapy on joints, and 4-following a clinical trial design. Case reports, animal design studies, review articles, non-original articles, conference abstracts, letters, book chapters, editorials, brief reports, and published full texts in non-English languages were excluded.

2.2. Data extraction

Two researchers (SH and MH-B) independently extracted the data from eligible papers including the name of the first author, publication year, country, mean age of the patients, duration of intervention, duration of follow-up, total number of patients, mean of Joint Score, mean joint pain score, and frequency of hemarthrosis. Any disagreement was resolved by the third author.

2.3. Study quality assessment

Two independent authors assessed the quality of the included studies based on Cochrane Collaboration Risk of Bias tool. This scale encompasses items related to randomization generation, allocation concealment, blinding of subjects, outcome assessment, incomplete outcome data, selective outcome reporting, and other sources of bias [17] (Figure 1).

2.4. Statistical analysis

This meta-analysis was set on aggregate data on randomized controlled trials. The collected data were entered into the Stata statistical software, version 13 (College Station, TX, USA, and analyzed by it. The change of before and after variables were calculated and the Hedges' g Standardized Mean Difference (SMD) was considered as the effect size for comparing the intervention and control groups regarding the changes in continuous variables (joint status and joint pain) on different occasions considering all of the evaluated joints (ankle, knee, and elbow) together. For each outcome variable, at first, mean difference between the two-time point was calculated for intervention and control groups, separately. Then, this syntax: "Metan N1 M1 S1 N2 M2 S2, lcols (Author Year)" was applied to illustrate the SMD of changes in the specified period between the intervention and control groups. [N1 = sample size in the control group; S1 = standard deviation in the control

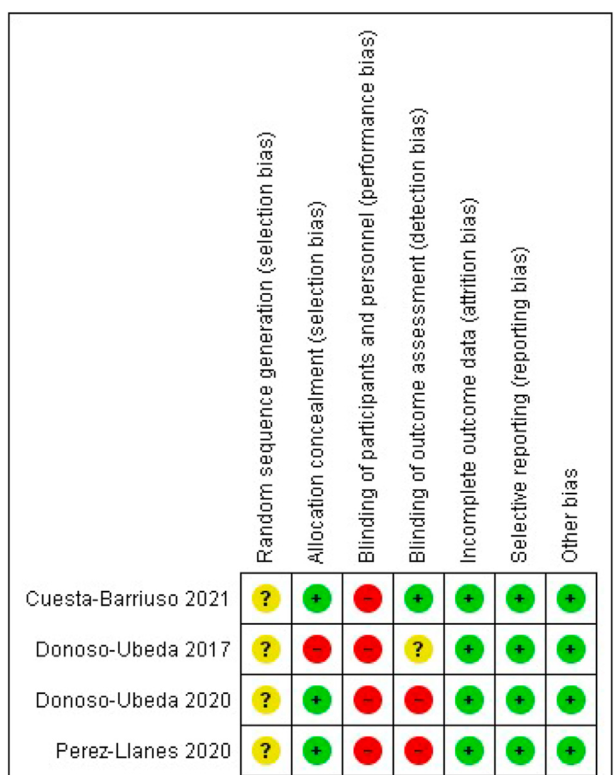

Figure 1. Quality assessment of the included studies.

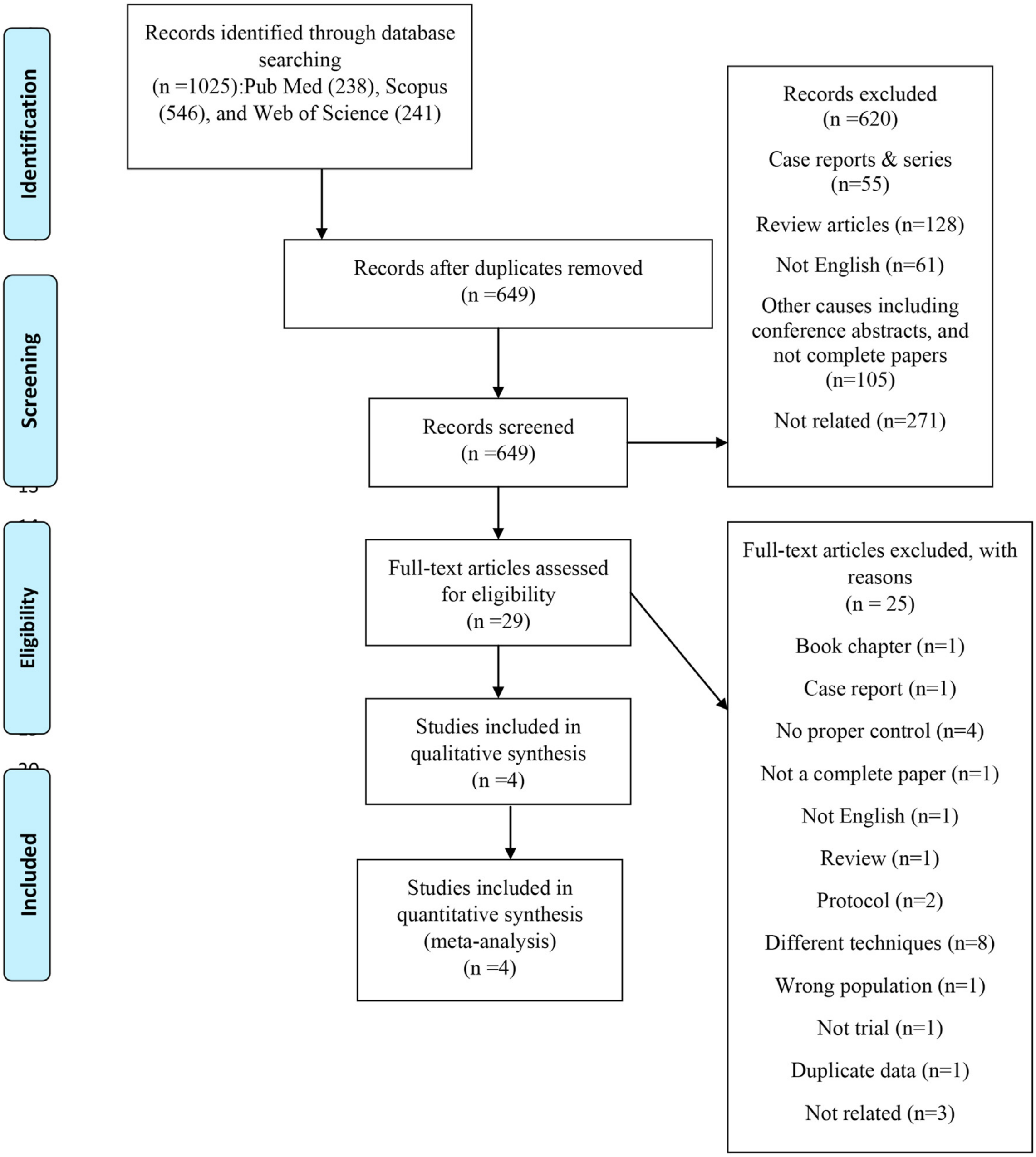

Figure 2. PRISMA flowchart of the study identification and selection process.

Table 1. Summary of the SMDs of the outcome variables between hemophilia patients with and without fascial therapy based on the established effect size classification.

Effect size classification	Very small	Small	Medium	Large	Very large	Huge
	0.01	0.2	0.5	0.8	1.2	2

Variables	**Effect size SMD (95%CI)**	**Class**
Load Joint pain		
Before and after fascial therapy	−0.61(−1.02, −0.21)*	Medium
Before and after follow up period	−0.13(−0.53, 0.27)	Very small
No-load Joint pain		
Before and after fascial therapy	−0.58(−0.88, −0.28)*	Medium
Before and after follow up period	−0.05(−0.35, 0.24)	Very small
Joint status		
Before and after fascial therapy	−0.49(−0.79, −0.19)*	Medium
Before and after follow up period	−0.54(−0.84, −0.24)*	Medium

* Statistically significant.

Table 2. General characteristics of the included studies.

Author	type A hemophilia	Severity	presence of inhibitor	Type of study	duration of follow up(month)	Total sample size(int/cont)	Type of Joint	outcome
Donoso-Ubeda, 2017 [23]	15(93.8%)	12(75%)	0	Nonrandomized CT	1	16(8/8)	knees, ankles	load pain, no load pain, Joint status, hemarthrosis
Donoso-Ubeda, 2020 [24]	42(64.6%)	55(84.6%)	5(7.6%)	RCT	5	65(33/32)	ankles	load pain, no load pain, Joint status, hemarthrosis
Cuesta-Barriuso, 2021 [22]	60(86.9%)	61(88.4%)	11(15.9%)	single-blind RCT	3	69(35/34)	elbow	no load pain, Joint status, hemarthrosis
Perez-Llanes, 2020 [25]	12(85.7%)	13(92.9%)	5(7.6%)	randomized pilot study	3	14(7/7)	elbow	no load pain, Joint status, hemarthrosis

group; M1 = Mean in the control group; N2 = sample size in the study group; S2 = standard deviation in the study group; M2 = Mean in the study group].

The established classification of the effect size are described in Table 1 [18, 19]. The degree of heterogeneity among the included studies was indicated by I-squared. The random effects model was used where heterogeneity was significant at 0.05 significant level or $I^2 > 50\%$ and fixed-effect model in cases that the heterogeneity was not significant. Besides, based on the characteristics of the included articles, a subgroup analysis was performed in order to explore the potential sources of heterogeneity if necessary. Pooled and individual data of the included surveys were depicted by Forest plots. In order to assess a potential publication bias, the Egger test was performed. The bias value and its confidence interval were reported. If the 95% confidence limit did not include the zero value or the significance level was less than 10%, this means that the studies have a publication bias [20]. The p-values extracted from this test were compared with the 0.05 significance level. Additionally, 95% Confidence Interval (CI) was provided for the bias

Table 3. Protocol for Myofascial Therapy for Treating Hemophilic Arthropathy of the Knee, Ankle, and elbow [25, 26].

Joint Knee & ankle	Maneuver	N	TP	TA	Time	Comments
	Superficial sliding of the anterior part of the leg	3	1	2	2 min	The strokes are performed, assisted by slight movements of dorsiflexion and plantar flexion by the patient.
	Superficial sliding of the anterior part of the thigh	3	3	–	2 min	None.
	Superficial sliding of the popliteal fascia	3	4	–	2 min	Movements are applied to the popliteal region. The maneuver is repeated 3 times.
	Superficial sliding of the posterior part of the thigh	3	1	2	2 min	The strokes are performed assisted by slight movements of dorsiflexion and plantar flexion.
	Superficial sliding of the posterior part of the leg	3	3	–	2 min	The 1st line is on the region of ease. The 2nd is on the outer thigh. The 3rd is on the inner thigh.
	Superficial sliding of the side part of the lower limb	3	3	–	2 min	The maneuver starts at the trochanteric region and ends in the posterior region of the lateral malleolus.
	Ankle joint complex	–	–	–	4–6 min	Overcome between 3 and 5 restriction barriers
	Anterior compartment of the knee	–	–	–	4–6 min	Hands crossed technique is applied to the anterior compartment of the knee.
	Thoracolumbar fascia	–	–	–	4–6 min	Hands crossed technique is applied to the thoracolumbar region
	Telescopic maneuver	–	–	–	5 min	This involves degravitation and slight traction of the lower limb.
Elbow						
	Longitudinal Surface	3	–	–	1–2 min	Longitudinal surface sliding maneuver over the superficial fascia in the anterior region of the arm and the forearm. The approximate duration of application is 30–45 s per stroke.
	Transverse sliding	3	–	–	1 min	Transverse sliding maneuver forthe flexor muscles of the wrist and fingers. Three sets of 15 slides.
	Transverse sliding	3	–	–	1 min	Transverse sliding maneuver for the biceps brachii muscle
	Longitudinal surface	3	–	–	1–1.5 min	Longitudinal surface slidingmaneuver over the superficial fascia in the posterior arm region. The approximate duration of application is 15–30 s per stroke.
	Transverse sliding	–	–	–	1 min	Transverse sliding maneuver over the brachial triceps tendon. Three sets of 15 slides
	Transverse sliding	–	–	–	1 min	. Transverse sliding maneuver for the pectoralis major muscle. Three sets of 15 slides
	Transverse sliding	–	–	–	1 min	Transverse sliding maneuver for the posterior axillary region (wide dorsal complex, subscapularis, teres minor, and teres major muscle) pectoralis major muscle. Three sets of 15 slides
	Induction maneuver	–	–	–	3–5 min	Induction maneuver of the fascia of the posterior axillary fold. Overcome 3 restriction barriers.
	Induction maneuver	–	–	–	3–5 min	Induction maneuver (crossed hands over the brachial region and forearm). Overcome 3 restriction barriers.
	Transverse planes	–	–	–	5 min	Maneuver of transverse planes for thecervicothoracic region. Overcome 3 restriction barriers
	Telescopic maneuver	–	–	–	5 min	Upper limb telescopic maneuver. Degravitation and slight traction

Type, Type of maneuver; N, number of strokes (total sliding maneuvers to be performed); TP, passive stroke (stroke made passively over the superficial fascias without assistance by the patient and usually applied in the sense of restraint); TA, assisted stroke (assisted strokes with the patient's cooperation); min, minutes.
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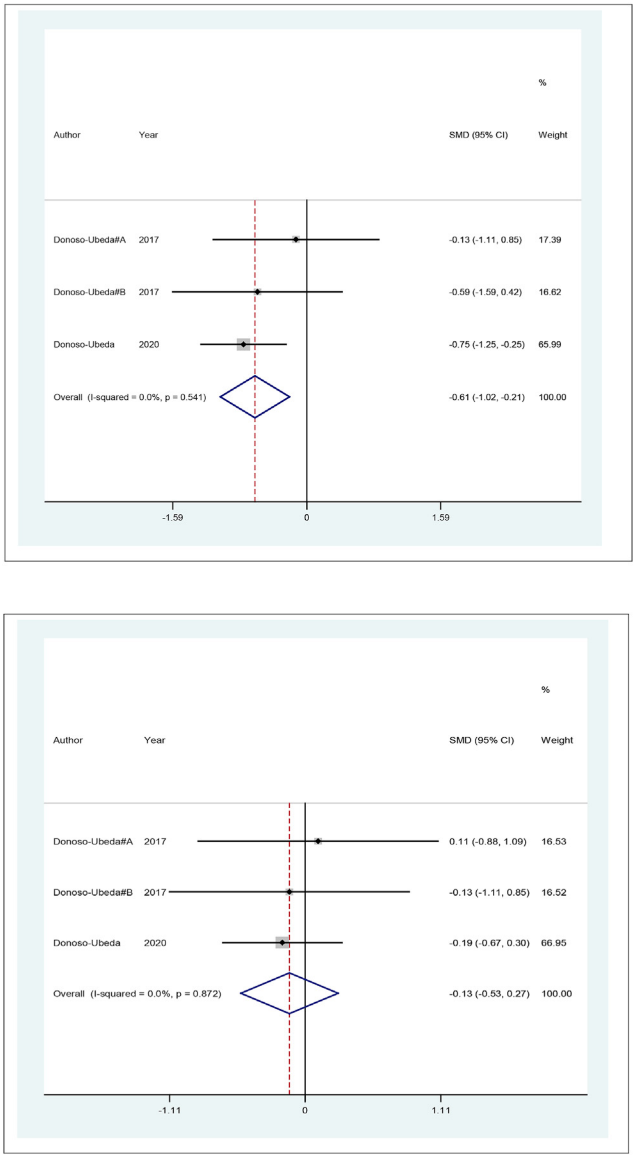

Figure 3. a: SMD of load joint pain change before and after fascial therapy between the intervention and control groups, b: SMD of load joint pain change before and after follow-up period between the intervention and control groups.

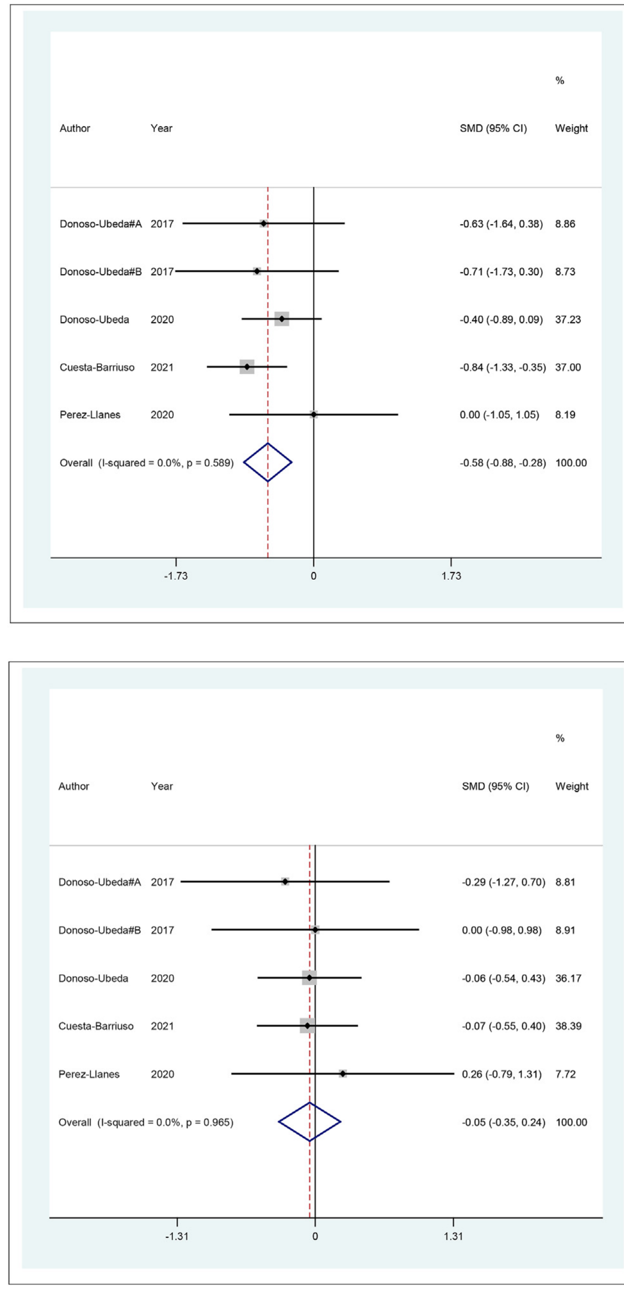

Figure 4. a: SMD of no-load joint pain change before and after fascial therapy between the intervention and control groups, b: SMD of no-load joint pain change before and after follow-up period between the intervention and control groups.

value. Sensitivity analysis was done, as well. The diagram was used for sensitivity analysis. Sensitivity analysis shows the effect of each study on the calculated effect size. In this diagram, by removing each of the studies separately, the effect size is calculated for the remaining studies, and its confidence intervals are also calculated. Also, based on this diagram, the degree of error of each study is determined in this way: if the removal of a study caused the 95% confidence interval to get wider, the deleted study is highly accurate [21].

3. Results

3.1. General characteristics

In the primary search, 1125papers were found, which reduced to 649 papers after removing the duplicates. After screening the titles and abstracts, 620 papers were excluded. Therefore, 29 full texts were screened. Finally, four papers met the inclusion criteria to be included in the analysis (Figure 2, PRISMA) [22, 23, 24, 25].

Based on the quality assessment, all evaluated studies achieved an acceptable grade rating according to Cochrane Collaboration Risk of Bias tool (Figure 1). The general characteristics of the included studies have been summarized in Table 2. These studies were conducted on 91 patients in the intervention group and 89 patients in the control group. All the patients had hemophilic arthropathy and all the included studies were conducted in Spain. The majority of the patients had type A, non-inhibitor, and severe type hemophilia. The mean ± Standard Deviation (SD) age of the patients was 40.55 ± 10.34 years and that of the controls was 38.97 ± 11.71 years ($p = 0.338$). All the patients in the case groups were provided with three myofascial release interventions through three physiotherapeutic sessions over a three-week period. Each session lasted for 45–60minutes. In all the studies, the physiotherapeutic intervention was performed by a physiotherapist with more than ten years of

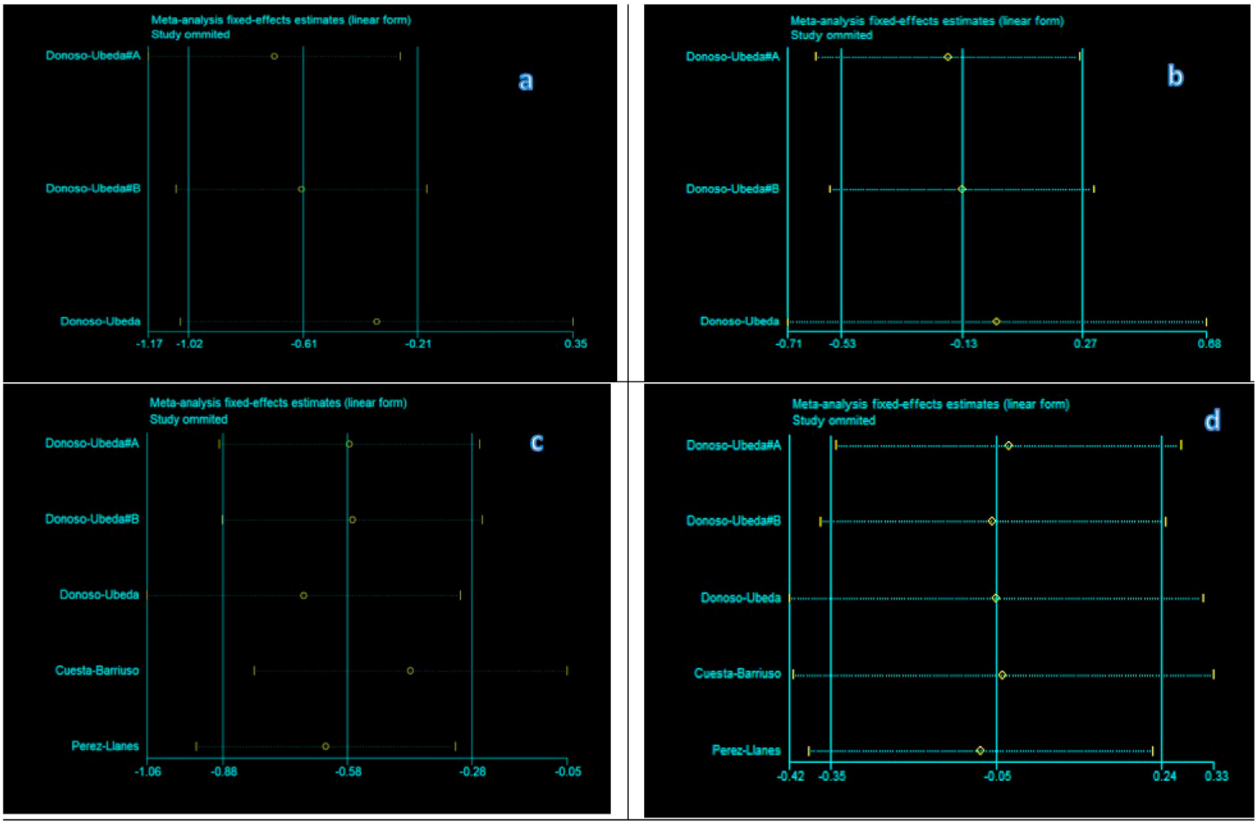

Figure 5. Sensitivity analysis a: load joint pain before and after fascial therapy in patients with hemophilic arthropathy, b: load joint pain before and after follow-up period in patients with hemophilic arthropathy, c: no-load joint pain before and after fascial therapy in patients with hemophilic arthropathy, d: no-load joint pain before and after follow-up period in patients with hemophilic arthropathy.

experience in fascial therapy and hemophilia through a designed protocol for patients with hemophilic arthropathy (elbow, knee, or ankle). This protocol consisted of six superficial maneuvers and four deep maneuvers for ankles and knees (Table 3) [26] and seven superficial maneuvers and four deep maneuvers for elbows (Table 3) [25]. joint status, as a validated tool, was utilized for optimal measurement of joint status and contained eight items including swelling, duration of swelling, muscle atrophy, crepitus of motion, extension and flexion loss, joint pain, strength, also the overall gait score. Its total score varied from 0 to 20per joint and the overall gait score ranged from 0-4, the higher the score, the greater degree of joint destruction [27]. In addition, the perception of pain was assessed using the visual analogue scale, a ruler ranging from zero which means no pain to ten which stands for the worst pain [22]. This method is wildly used for the perception of pain in patients with hemophilic arthropathy [22, 28]. The pain was measured under two conditions; i.e., under load bearing and non-load bearing [24].

3.2. Main outcomes

3.2.1. Hemarthrosis

Meta-analysis of the data related to the safety of MFT was not possible due to the limited number of studies reporting the accurate frequency of hemarthrosis at baseline and after the intervention. Thus, the results of the hemarthrosis were only reported without any analysis. A trial conducted [23]on patients with knee and ankle arthropathy in 2017 indicated that none of the patients in the intervention group developed spontaneous hemarthrosis during the trial and the follow-up period. In contrast, one patient in the control group developed hemarthrosis during the trial and three patients during the follow-up period. Another trial in 2020(24) revealed a significant reduction in the frequency of ankle hemarthrosis in the intervention group compared to the controls. Moreover, none of the patients with elbow arthropathy who underwent MFT developed hemarthrosis during the intervention up to three months [23, 25]. Furthermore, a trial with a larger number of patients affected by elbow arthropathy demonstrated a decrease in the frequency of joint bleeding [22, 24].

3.2.2. Joint pain with load

The results revealed a significant difference between the hemophilia patients with and without MFT regarding the SMD of changes from baseline to three weeks after MFT (SMD = -0.61, 95% CI: -1.02, -0.21; heterogeneity was not significant: $I^2 = 0$, p = 0.541). However, the change observed from the baseline to the follow-up period was not statistically significant (SMD = -0.13, 95% CI: -0.53, 0.27; heterogeneity was not significant: $I^2 = 0$, p = 0.872) (Figure 3 a, b). Sensitivity analysis showed that the study carried out by Donoso–Ubeda et al. [24] had the greatest effect, as the removal of this study caused the pooled analysis to be insignificant(Figure 5 a, b).

3.2.3. Joint pain without load

The results revealed a significant difference between the hemophilia patients with and without MFT regarding the SMD of change between the beginning of therapy and three weeks later (SMD = -0.58, 95% CI: -0.88, -0.28; heterogeneity was not statistically significant: $I^2 = 0$, p = 0.589). However, the change between baseline and after the follow-up period was not statistically significant (SMD = -0.05, 95% CI: -0.35, 0.24; heterogeneity was not statistically significant:$I^2 = 0$, p = 0.965) (Figure 4 a, b). Sensitivity analysis disclosed that the studies performed by Donoso-Úbeda et al. [24]and Cuesta-Barriuso et al. [22]had the greatest effects on the pooled analysis(Figure 5 c, d).

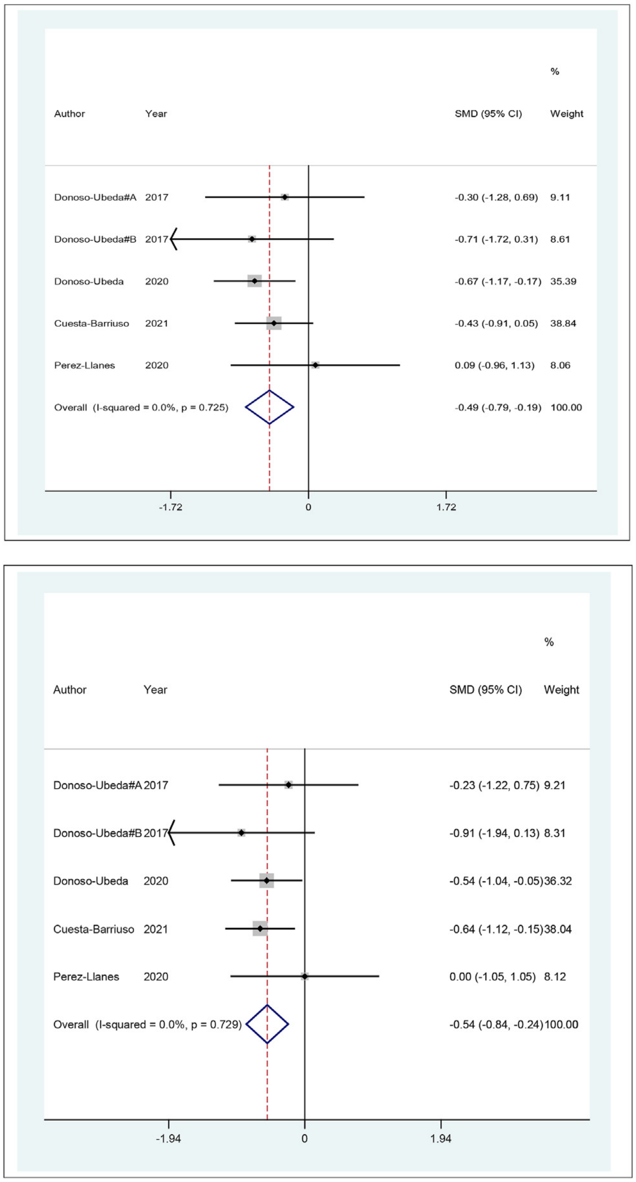

Figure 6. a: SMD of joint status change before and after fascial therapy between the intervention and control groups, b: SMD of joint status change before and after follow-up period between the intervention and control groups.

3.2.4. Joint status

The results indicated a significant difference between the hemophilia patients with and without MFT regarding the SMD of change between the beginning of therapy and three weeks later (SMD = -0.49, 95% CI: -0.79, -0.19; heterogeneity was not statistically significant: $I^2 = 0$, $p = 0.725$). The change between baseline and after the follow-up period was also statistically significant (SMD = -0.54, 95% CI: -0.84, -0.24; heterogeneity was not statistically significant:$I^2 = 0$, $p = 0.729$) (Figure 6 a, b). Furthermore, sensitivity analysis demonstrated that the research conducted by Donoso–Ubeda et al. [24] and Cuesta-Barriuso et al. [22]had the greatest effect on the pooled analysis (Figure 7 a, b).

4. Discussion

In this meta-analysis, the effectiveness of a physiotherapeutic protocol using myofascial release was assessed in patients with hemophilic arthropathy. Overall, the data of 91 patients with hemophilic arthropathy in the intervention group were compared with those of 89 patients with hemophilic arthropathy in the control group. MFT was done over three 45-60-min sessions during three weeks and was found to be effective in reducing both load bearing and non-load bearing joint pain in hemophilic patients. Moreover, myofascial release improved the patients' joint health status, which remained for one-five months in different trials.

One of the major concerns associated with using physiotherapeutic techniques in hemophilic patients is hemarthrosis. The first bleeding usually occurs in 1–3 years of life [29]. Chang et al. reported that severe arthropathy increased in hemophilia patients above 30 years old [30]. Joint bleeding begins a cascade of inflammatory responses, which induces the joint degenerative process that hurts the synovium, cartilages, and bones and eventually causes joint deformity [31]. The safety of the majority of manual interventions was demonstrated by a reduction in the frequency of hemarthrosis in these patients [32, 33, 34]. The results indicated that not only MFT did not cause joint bleeding [23, 25], but it also reduced the frequency of hemarthrosis in some cases [22, 24]. It should be mentioned that the included patients were hemophilic ones receiving prophylactic or on-demand factor replacement therapy, which might have influenced the occurrence of hemarthrosis. During acute joint bleeding it is important to replace deficient factor as soon as possible. In patients with the presence of inhibitors administration of activated prothrombin complex concentrate or recombinant activated factor VIIa is recommended [35]. However, due to the lack of data in some studies, subgroup analysis was not possible.

Pain is the most crucial factor affecting functionality and quality of life in hemophilia patients. In a study it is found that pain was more prominent in ankle joint followed by knee pain, and elbow pain [29]. One of the mechanisms of pain reduction is modulating neural reflexes via the stimulation of special fascial receptors [24]. The MFT method usually contains bearing a small load on the soft tissue and manipulation of fascia protects the healthy tissue. This technique promotes the collagen fiber orientation and efficiently relieves the joint pain [12, 36]. Based on the results of this meta-analysis, both load and non-load bearing joint pains were significantly decreased three weeks after MFT. Improvement of pain perception in hemophilic arthropathy was also achieved through other physiotherapeutic interventions such as manual therapy, mobilization, and joint traction performed twice a week over 6–12 weeks [32, 37, 38]. Manual therapy can decrease pain through the reduction in inflammatory markers, decrease pain sensitivity of nervous system, modification of cortical areas involved in pain processing, and finally psychological factors [39]. Physical exercise also mentioned as a tool for reducing perception of pain in hemophilia patients, also it can increase the production of synovial fluid and enhance the diffusion of nutrients to cartilages [29]. Moreover, in an umbrella review it is demonstrated that exercise can improve physical aspect of life in hemophilia patients with minimal side effects [40]. Exercise will improve the muscle power and decrease the risk of atrophy progression [40]. Also, in a recent meta-analysis it was recommended that both therapeutic exercise and myofascial therapy can improve joint health status in hemophilia patients [41]. Nonetheless, the present study results revealed a more rapid effect of MFT on pain reduction (after only three sessions over three weeks). On the other hand, pain improvement was maintained for six months in the above-mentioned studies, while the results of the pooled analysis did not support the remaining of pain improvement for more than three weeks during the follow-up period (one-five months). The higher frequency of the interventions applied in those methods compared to the MFT protocol might have resulted in a more sustained improvement in pain perception. This issue can be a topic for future lines of research in this area.

In a systematic review conducted in patients with osteoarthritis it was found that manual therapy can reduce the joint pain and increase range of motion and functionality in knee osteoarthritis [42]. Also, it was demonstrated that manual therapy can be useful in patients with rheumatoid arthritis and knee joint involvement. Post isometric relaxation and low-grade joint mobilization as parts of manual therapy can reduce joint pain and increase functionality in rheumatoid arthritis with knee joint involvement [43]. Moreover, in patients with fibromyalgia it was

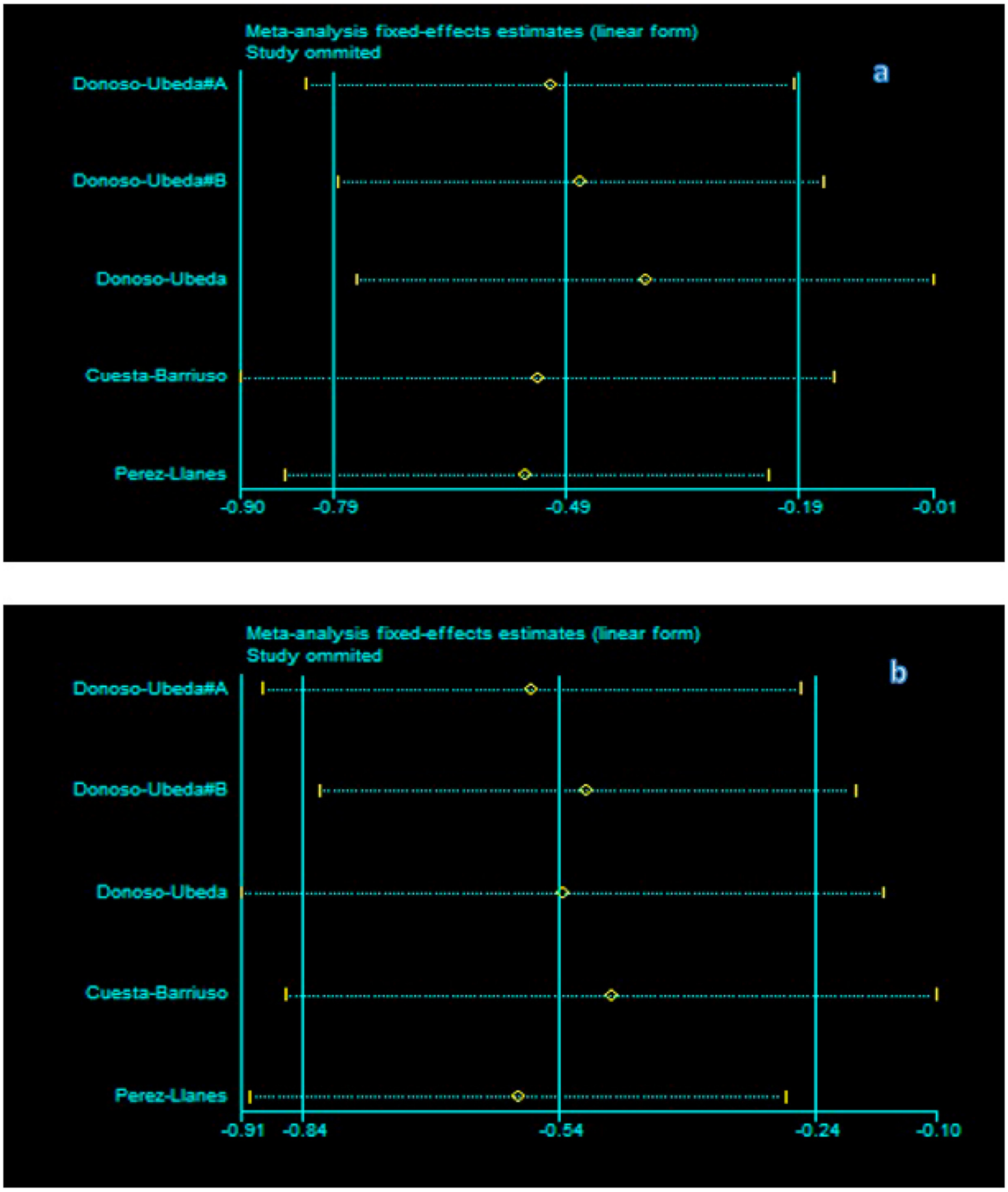

Figure 7. Sensitivity analysis, a: Joint status before and after fascial therapy in patients with hemophilic arthropathy, b: Joint status before and after follow-up period in patients with hemophilic arthropathy.

disclosed that manual therapy reduced both delayed and immediate perception of pain [44].

The joint status is a beneficial measure for evaluating the changes in joint health after employing a new therapy or even after the disease progression [45, 46]. Based on the current study findings, the joint status was significantly improved three weeks after MFT, which remained until the follow-up period. It seems that the joint status improves as a result of pain alleviation, mobility promotion, and decreased joint crepitation [24]. Myofascial release improves arterial function and enhances the vascular endothelial function via increasing levels of plasma nitric oxide [14, 15]. Also, MFT can modulate the activity of autonomic nervous system and increase the joint flexibility and range of motion [14]. All of these process are responsible for promoting joint status. In comparison with pain perception, joint status is less subjective and considers different aspects of joint health. Hence, this score seems to be representative of the joint health status, and retention of the improvement for longer durations indicates the promising results of MFT. A recently published study on the effect of fascial therapy in patients with hemophilic elbow arthropathy showed a significant improvement in the physical and mental health components of quality of life measured by the Short-Form Health Survey-36 (SF-36) questionnaire alongside a decrease in pain intensity and an improvement in the joint status [47].

The strong points of the present study were pooling the available data and achieving larger samples on the effect of MFT on hemophilic arthropathy in adult patients mostly affected by severe hemophilia. However, some limitations must be considered in interpreting the results. First, the number of relevant published papers was limited. So, there were small number of publications to be analyzed and all the included studies were related to the clinical centers of Spain. But, the studies were multicenter. Secondly, only English-language studies were included in this review. Thirdly, due to the lack of data, subgroup analysis was not possible for some potentially confounding factors such as type of the involved joint and type of the regimen for coagulation factor replacement therapy (prophylaxis or on-demand). Fourthly, with regard to safety, because the frequency of hemarthrosis could not be analyzed as a quantitative value, the results of the published papers were only reported without conducting any analysis. Finally, the included trials were single blinded. In other words, the patients were aware of receiving interventions, which could potentially increase the risk of bias.

In conclusion, in addition to pharmacological and prophylactic treatment, this meta-analysis showed that MFT can be an effective intervention improving the joint status and decreasing pain perception in patients with hemophilic arthropathy. Consequently, it can play an important role in achieving higher functionality and quality of life in these patients. However, due to the small number of studies and other limitations, further well-designed trials and updated meta-analysis are needed for more accurate results and interpretation.

Declarations

Author contribution statement

All authors listed have significantly contributed to the development and the writing of this article.

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Data availability statement

The authors are unable or have chosen not to specify which data has been used.

Declaration of interest's statement

The authors declare no conflict of interest.

Additional information

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