European Journal of Physical and Rehabilitation Medicine 2023 December;59(6):763-71
DOI: 10.23736/S1973-9087.23.07944-3

ORIGINAL ARTICLE

Foam roller-based self-induced myofascial therapy in patients with hemophilic knee arthropathy: a multicenter, single-blind, randomized clinical study

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ABSTRACT

BACKGROUND: Hemophilia is a congenital coagulopathy characterized by degenerative joint damage. Self-induced myofascial therapy aims to decrease pain and improve tissue mobility, functionality and proprioception.
AIM: The aim of this study was to evaluate the safety and efficacy of self-induced myofascial release in patients with hemophilic knee arthropathy.
DESIGN: This is a randomized clinical study.
SETTING: This study was carried out in different patient associations.
POPULATION: Fifty-two patients with hemophilia were included in the study.
METHODS: Patients were randomized to the experimental group (daily home protocol of foam roller-based self-induced myofascial therapy for 8 weeks) or the control group (no intervention). The variables were the frequency of hemarthrosis (self-reporting), pain intensity (visual analog scale), range of motion (goniometry) and muscle strength (dynamometry). All variables were evaluated at baseline, post-treatment and after a 10-week follow-up.
RESULTS: The patients included in the experimental group showed significant improvements in terms of a decrease in frequency of hemarthrosis (mean difference [MD]=-0.61; 95% confidence interval [CI]: -0.81; -0.41) and pain intensity (MD=-0.33; 95% CI: -0.48, -0.18), increased range of motion (MD=0.88; 95% CI: 0.39; 1.37), strength in quadriceps (MD=0.88; 95% CI: 0.39; 1.37). (MD=12.39; 95% CI: 3.44; 21.34) and hamstrings (MD=7.85; 95% CI: 0.60; 15.11). There were intergroup differences in the frequency of hemarthrosis (F=14.51; P<0.001), pain intensity (F=9.14; P<0.001) and range of motion (F=13.58; P<0.001).
CONCLUSIONS: Self-induced myofascial therapy can be an effective complementary technique in the treatment of patients with hemophilic arthropathy. Self-induced myofascial therapy can reduce the frequency of knee hemarthrosis in patients with hemophilia. This technique can improve pain intensity and range of motion in patients with hemophilic knee arthropathy.
CLINICAL REHABILITATION IMPACT: Hemophilic knee arthropathy is characterized by chronic pain, decreased range of motion, and periarticular muscle atrophy. Foam roller-based self-induced myofascial therapy can reduce the frequency of hemarthrosis and pain intensity and improve range of motion in patients with hemophilic arthropathy. Foam roller-based self-induced myofascial therapy is safe and effective in the treatment of patients with hemophilia. The inclusion of self-induced myofascial therapy exercises in the approach to degenerative joint pathologies may be an effective and safe treatment option.

(*Cite this article as:* Donoso-Úbeda E, Pérez-Llanes R, Meroño-Gallut J, Ucero-Lozano R, Cuesta-Barriuso R. Foam roller-based self-induced myofascial therapy in patients with hemophilic knee arthropathy: a multicenter, single-blind, randomized clinical study. Eur J Phys Rehabil Med 2023;59:763-71. DOI: 10.23736/S1973-9087.23.07944-3)

KEY WORDS: Hemophilia A; Hemophilia B; Knee joint; Physical therapy modalities; Hemarthrosis; Range of motion, articular.

Hemophilia is a congenital clotting disorder caused by a deficiency or absence of one of the clotting factors. Depending on the deficiency factor, there are two types of hemophilia: FVIII (hemophilia A) and FIX (hemophilia B).[1] The severity of hemophilia depends on the plasma concentration of such clotting factors: mild (5-40%), moderate (1-5%) or severe (<1%).[2] Although hemophilia is a hematological disease, the development of hemarthrosis is the most relevant clinical manifestation mainly affecting knees, ankles and elbows.[3]

The recurrence of hemarthrosis in the same joint leads to synovial hypertrophy, hemosiderin deposition, cartilage destruction and alterations in the structure of the subchondral bone. Such hemosiderin deposition can stimulate further synovial hypertrophy and inflammation.[4] The development of hemarthrosis induces chondrocyte apoptosis,[5] which alters cartilage matrix regeneration. Initially expressed by hypertrophic synovium, hypervascularization occurs on the synovial tissue, increasing the risk of further bleeding, and the onset of inflammatory changes. These inflammatory changes contribute to cartilage damage, through the production of enzymes and cytokines that destroy the tissue, leading to joint destruction.[6] A recent study[7] has shown how iron is involved in cartilage injury through the regulation of the expression of FGF23 and SOX9 in chondrocytes in patients with hemophilia who have developed hemarthrosis. A high level of COL-18N has been observed in patients with hemophilia A, and it can be used as a potential marker to monitor the development of arthropathy, allowing the best treatment to be adapted to prevent further joint damage.[8] Recurrent hemarthrosis leads to the development of a degenerative and irreversible process known as hemophilic arthropathy.[9] As a result, hemophilic arthropathy is accompanied by pain, loss of joint range and muscle atrophy, among other alterations. This arthropathy is characterized by cartilage destruction, chronic pain, decreased joint range and impaired functionality.[10]

Joint pain associated with hemophilic arthropathy adversely affects the perceived quality of life of this population.[11] A number of physiotherapy techniques such as joint traction[12] or the application of electromagnetic pulse fields[13] have shown to be effective in improving pain perception in people with hemophilic knee arthropathy.

Myofascial therapy is a form of manual therapy applying sliding techniques and gentle sustained pressure to mobilize the fascial complex. This technique aims to reduce pain and improve tissue mobility, functionality and proprioception.[14] Self-induced myofascial therapy using a foam roller is a technique used to increase local blood flow thanks to the thixotropy of the fascial tissue. The pressure exerted by the foam roller on the patient's tissues causes their deformation and alters their viscosity. In this way, scar tissue adhesions are reduced.[15, 16] The technique is performed by rolling the weight of the area to be treated on the roller, thus being a self-massage.[15] The use of myofascial self-release exercises has shown its effectiveness in reducing pain in patients with hip osteoarthritis[17] and plantar fasciitis,[18] also improving the range of motion in the latter case. Although a recent cohort study[19] has shown the safety and efficacy of a self-induced myofascial therapy protocol in patients with knee arthropathy, to date there have been no multicenter randomized clinical studies confirming the efficacy of this technique.

The main objective of this study was to investigate whether the application of foam roller-based self-induced myofascial therapy can improve the frequency of hemarthrosis, pain intensity, range of motion and quadriceps strength in patients with hemophilic knee arthropathy.

Materials and methods

Study design

This is a randomized, multicenter, single-blind clinical study with follow-up period. The study was approved by the Research Ethics Committee of the University of Murcia, Murci, Spain (ID: 2428/2019). The research project was registered with the International Registry of Clinical Trials (www.clinicaltrials.gov; ID: NCT05108480. First registration: 05/11/2021). Patients who met the selection criteria were informed verbally and in writing about the objectives, risks and benefits of the intervention. All patients signed an informed consent document, in accordance with the Declaration of Helsinki. The patients were recruited from eight cities of Spain (A Coruña, Bilbao, Burgos, Granada, Madrid, Murcia, Valladolid, Vigo) between the months of February and July 2022.

Participants

The inclusion criteria were: 1) patients with a diagnosis of hemophilia A or B; 2) severe hemophilia phenotype; 3) patients over 18 years of age; and 4) with a diagnosis of bilateral hemophilic knee arthropathy and more than 3 points on the Hemophilia Joint Health Score.[20] The exclusion criteria were: 1) patients who had developed knee hemarthrosis in the three months preceding the study; 2) patients unable to walk; 3) patients with severe functional limitations in the upper limbs that prevented carrying out

the exercises; 4) failure to complete 80% of the sessions; and 5) failure to sign the informed consent document.

Intervention

Patients included in the experimental group completed the exercises described in the protocol designed by Meroño-Gallut *et al.*[21] A foam roller measuring 30 cm in length and 15 cm in diameter and an 8-cm diameter ball were used. On the first day, the physiotherapist in charge of supervising the intervention explained the intervention to patients. On a weekly basis, the researcher conducted a follow-up on the sessions by a video call interview with the patients, responding to any doubts or questions raised by them. Depending on the onset of pain or limitations in the upper or lower limbs, the researcher adjusted the exercises to enable completion of the exercises with compensations.

The experimental group patients carried out daily 15-minute sessions, for 8 weeks. All participants had access to a mobile application designed by the research group (He-Foam®; InHeFis, Murcia, Spain) where they could watch videos of all the exercises, find instructions and solve doubts. The exercise protocol for the knee region included 5 exercises:

• foam rolling to release the posterior leg region – the patient, sitting on the floor, placed the foam roller at the most distal area of the leg. He or she then completed 15 longitudinal slides. If the patient's clinical condition so allowed, rolls continued while crossing the contralateral leg over the other;

• foam rolling to release the hamstring region – the patient, sitting on the floor, placed the roller under the hamstring region. First 10 unilateral rolls and another 10 bilateral rolls over the back of the thighs;

• adductor release using a ball – the patient, sitting on a chair, placed the ball between the thighs. Circular movements were made with one leg at the most distal area, the middle area and the most proximal area of the thigh. Then 5 slides on each region while exerting gentle pressure;

• foam rolling to release the abductor muscles – the patient in lateral decubitus position with the roam roller under the side of the thigh. The patient performed 10 longitudinal rolls reaching as far as possible;

• foam rolling to release the pelvitrochanteric muscles – the patient sitting on the foam roller, with the affected leg crossed over the contralateral leg and the weight of the body on the affected region. Then 15 slow longitudinal movements.

The application made it possible to measure the degree of compliance with the intervention. When performing the intervention, the date and time were recorded. All interventions were supervised by the same physiotherapist, with more than 15 years of experience in the treatment and assessment of patients with congenital coagulopathies. We specifically asked the participants to stop foam rolling after the intervention stage was complete. All patients received regular hemostatic monitoring at their referral hospital. The therapeutic regimen of the patients prescribed by their hematologist was not modified.

To increase precautions and improve the safety of the protocol used, in the first session the exercises were performed under the supervision of a physiotherapist. In this first session, the necessary time was spent so that the patient became familiar with the exercises, and they understood the correct execution and the necessary adaptations to perform the protocol without risk or pain. In addition, the patients had direct telephone/video contact throughout the study phase to talk to the physiotherapist and to correct or adapt the exercises depending on the patient's clinical situation each day.

Outcomes

Three evaluations were carried out: at baseline (T0), at the end of the experimental stage (T1), and after a 10-week follow-up period (T2). The primary variable was pain intensity. Secondary variables were the frequency of knee hemarthrosis, range of motion, and quadriceps and hamstring muscle strength.

• Pain intensity – measured using the visual analog scale.[22] This scale has shown a high intraobserver reliability (ICC: 0.99).[23] It consists of a continuous horizontal 100-mm line, where the end points define extreme limits for "no pain" and "maximum perceived pain intensity." The scores range from 0 (no pain) to 10 points (maximum perceived pain).

• Frequency of hemarthrosis – the development of hemorrhagic complications was evaluated through weekly follow-up interviews *via* video call. The rater had a questionnaire with closed-ended questions to be completed with closed-ended answers. These questions referred to the main clinical manifestations of hemarthrosis: aura, previous trauma, pain, functional disability, swelling, heat, etc. Likewise, in case of bleeding, data on location, duration, evolution and functional characteristics were collected.

• Range of motion – knee mobility was assessed with a universal goniometer[24] in the sagittal plane. This instrument has shown good intraobserver reliability (ICC: 0.91-0.99).[25] The fibula was the distal reference point. Mobility was measured under no-load and pain-free active range

of motion (ROM) conditions. Three measurements of full knee ROM were taken, the average value being recorded.[26] Degrees are the unit of measurement of this instrument (the higher the degree, the greater the mobility).

• Muscle strength – evaluated with a dynamometer (model Lafayette Manual Muscle Tester 01165). This instrument has shown good intra-rater reliability (ICC>0.70).[27] The patients first practiced to become familiarized with the test in order to exert maximum force against the dynamometer, which was held by the evaluator.[28] The quadriceps and hamstring muscle strength was evaluated, prompting all patients with the same verbal instructions. Each patient performed two 5-second maximum isometric contractions, with a 30-second break between them. The mean value of the two contractions was used for the force analysis.[29] The unit of measurement of this measuring instrument is N/cm^2, where the higher the score, the greater the muscle strength.

Before the study, the intraobserver reliability of the measurement instruments used was calculated. The evaluator measured the range of motion and muscle strength variables in seven subjects without hemophilia. High intraobserver reliability was observed in all variables (ICC>0.80). In the same way, the interobserver reliability was calculated to obtain the minimum detectable change (SD_{pre}).

Sample size

The sample size was calculated using the statistical software G*Power (version 3.1.9.2; G-Power, Brunsbüttel, Germany). Assuming a low effect size (d=0.30)[30] with an alpha level (type I error) of 0.01 and a statistical power of 95% (1-β=0.95), a sample size of 54 patients with hemophilic knee arthropathy was estimated.

Randomization and blinding

Randomization was performed using a computerized randomization procedure by permuted blocks of 4 subjects at each recruitment center. The 6 possible sequence alternatives were modified in each block. A social worker from a Hemophilia Association, blinded to the study objectives and characteristics, assigned a code to each patient during the randomization process and carried it out. To ensure the blinding of the person in charge of allocation, the sequence of blocks permuted with the letters A and B was provided so that the patients identified with code numbers were assigned to each of the study groups.

The experimental group patients (N.=26) completed the self-induced myofascial release exercises on a daily basis for 8 weeks. The control group patients (N.=26) did not undergo any intervention, while they were asked to continue as before with their usual daily activities. The therapeutic regimens prescribed by the hematologist were not changed, each patient continuing with their usual prophylactic or on-demand treatment.

All evaluations were performed by the same evaluator, blinded to patient group allocation. The evaluator measured all the subjects of both groups, under the same conditions and using the same protocol. To ensure the blinding of the evaluator, he or she was only aware of the patient's numerical code without being aware of the patient's study group allocation. In addition, the patients were evaluated randomly without an established order depending on the study group. In this way, the evaluator was at no point aware of the assignment of the patients being evaluated.

Statistical analysis

Statistical analyses were performed with version 19.0 of the SPSS statistics software for Windows (IBM Company, Armonk, NY, USA). According to *a-priori* sample size calculation parameters, the statistical significance was set at P<0.01 for a 99% confidence interval (CI). An intention-to-treat analysis was carried out. The intra- and inter-rater reliability analysis was performed with the two-way random intraclass correlation coefficient. Fisher's Exact Test was employed to analyze the differences in the qualitative variables between groups. Normality was assessed with the Shapiro-Wilk Test. For the parametric data, the mean and standard deviation were calculated, with the Student's *t*-test for independent samples. For the non-parametric data, the median and the interquartile range were calculated using the Mann-Whitney U Test. Although some data were not normally distributed, F tests are robust in terms of type I error, and regardless of the manipulated conditions are considered a valid option for non-parametric distributions.[31] The intergroup effect was calculated with repeated measures ANOVA. Moreover, the Mauchly Test was developed to assess sphericity, and the Greenhouse-Geisser correction was employed when the sphericity assumption was not fulfilled. The effect size of the F tests was analyzed using the eta-squared coefficients (η^2) and was interpreted as a small (η^2=0.01), medium (η^2=0.06) and large (η^2=0.14) effect size.[32] The minimum detectable change (MDC) was obtained by estimating the standard error of measurement (SEM) with the formula: $SEM=SDpre\times\sqrt{1-ICC}$.[33] The formula ($MDC=Z\text{-score}\times\sqrt{2}\times SEM$) was used to obtain the MDC. The confidence level was set at 99% (Z score=2.57).[34] Lastly the proportion of patients whose

change after the intervention exceeded the value indicated by the MDC was calculated.

Results

Sixty-five patients with hemophilia A and B were invited to participate in the study. Thirteen patients were excluded for various reasons: 1) knee hemarthrosis in the months preceding the study (N.=4); 2) scheduled orthopedic surgeries (N.=3); 3) severe functional limitations in upper limbs (N.=3); 4) inability to walk (N.=2); and 5) lack of interest in the study (N.=1). Ultimately, 52 patients with hemophilic knee arthropathy were included in the study and randomized to the study groups. The flow chart of the patients included in the study is shown in Figure 1.

The mean (SD) age of the 52 patients included in the study was 38.35 (8.58) years. The mean joint damage of the knees, measured with Hemophilia Joint Health Score, was 7.54 (2.74) points. Most patients had a diagnosis of hemophilia A (82.7%) and were undergoing prophylactic pharmacological treatment with clotting factor concentrates (76.9%). On the other hand, 19.2% of the patients presented antibodies to the clotting factor (inhibitors) during the study phase. The degree of compliance with the intervention was 97.06% (4.41). The clinical and sociodemographic data of the patients are shown in Table I.

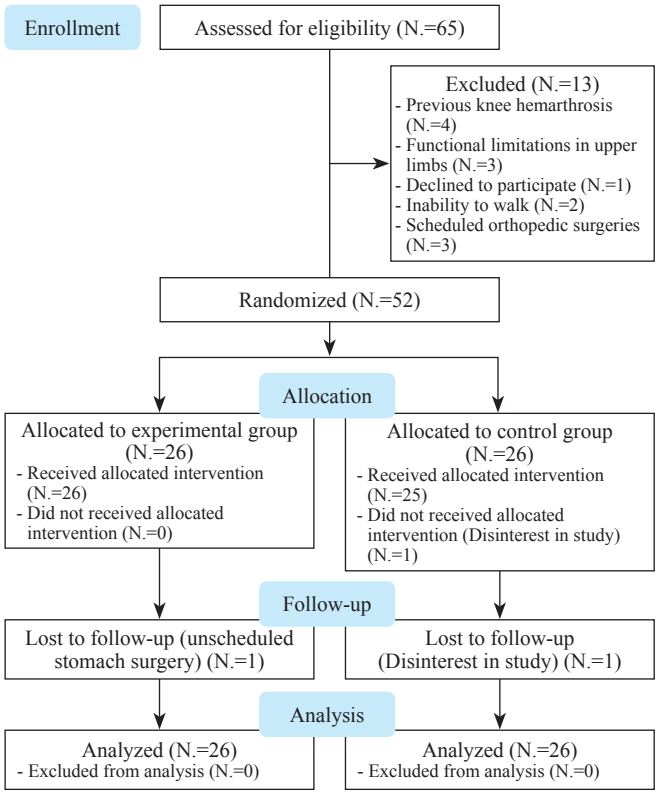

Figure 1.—Study flowchart.

Pain intensity

When analyzing the intergroup effect, we observed statistically significant differences (F[1.82;186.05]=37.14; P<0.001). Table II shows the results of the repeated measures analysis. In the pairwise comparison analysis, there were significant changes in T1-T0 (P<0.001; 99% CI: -0.33; -0.07) and T2-T0 (P<0.001; 99% CI: -0.36; -0.06). Table III shows the results of the pairwise comparison analysis. The value of the minimum detectable change was 0.52 points. Changes greater than the MDC after the intervention were reported in 28.84% of experimental group patients. The results of the calculation of the minimum detectable change are shown in Table IV.

Frequency of hemarthrosis

There were statistically significant differences in the intergroup effect of the frequency of knee joint bleeding (F[1.65;168.45]=14.51; P<0.001). There were significant differences in T1-T0 (P<0.001; 99% CI: -0.49; -0.15) and T2-T0 (P=0.009; 99% CI: -0.42; -0.003).

TABLE I.—*Descriptive analysis of the sample.*

Variables	Experimental group N.=26 (%)	Control group N.=26 (%)	P value
Age (years)	38.15 (10.83)*	38.54 (5.74)*	0.87**
Weight (kg)	82.62 (11.06)*	84.42 (4.54)*	0.44**
Height (cm)	173.15 (5.67)*	177.38 (4.65)*	0.00**
Body Mass Index (kg/m²)	27.57 (3.75)*	26.88 (1.95)*	0.40**
Joint health (0-20)	6.00 (5.25)†	7.50 (4.00)†	0.77‡
Joint pain	2.20 (1.99)*	2.16 (1.30)*	0.92**
Frequency of hemarthrosis	0 (1)†	0 (1)†	0.48‡
Range of motion	134 (27.5)†	123.5 (15.75)†	0.01‡
Quadriceps strength	284.40 (105.55)†	270.35 (49.15)†	0.72‡
Hamstring strength	255.70 (61.65)*	254.62 (24.90)*	0.90**
Type of hemophilia			
Hemophilia A	20 (72.4)	23 (88.5)	0.46§
Hemophilia B	6 (27.6)	3 (11.5)	
Type of treatment			
Prophylactic	22 (79.3)	21 (80.8)	0.32§
On demand	4 (20.7)	5 (19.2)	
Inhibitors			
Yes	20 (76.9)	22 (84.6)	0.72§
No	6 (23.1)	4 (15.4)	

N.: number of subjects.
*Mean (standard deviation) was applied; **Student's *t*-test for independent samples was performed; †median (interquartile range) was used; ‡Mann-Whitney U Test was utilized; §Fisher's Exact Test.

TABLE II.—*Mean (and 99% confidence interval) and intergroup analysis of study.*

Variables	Experimental group Mean [SD] (99% CI)	Control group Mean [SD] (99% CI)	Between-group change score
Joint pain (range 0-10)			
Baseline	2.20 [1.99] (1.46; 2.93)	2.16 [1.30] (1.68; 2.65)	F=9.14; P=0.000*
Post-treatment	1.86 [2.05] (1.10; 2.62)	2.09 [1.32] (1.60; 2.59)	η^2=0.08
Follow-up	1.80 [1.90] (1.09; 2.50)	2.13 [1.31] (1.64; 2,61)	
Frequency of hemarthrosis (number)			
Baseline	0.65 [0.76] (0.37; 0.94)	0.75 [0.76] (0.47; 1.03)	F=14.51; P=0.000*
Post-treatment	0.06 [0.19] (0.00; 0.11)	0.71 [0.72] (0.44; 0.98)	η^2=0.12
Follow-up	0.19 [0.39] (0.04; 0.34)	0.78 [0.77] (0.50; 1.08)	
Range of motion (degree)			
Baseline	123.19 [25.44] (113.75; 132.63)	121.23 [9.69] (117.63; 124.83)	F=13.58; P=0.000*
Post-treatment	124.07 [24.94] (114.82; 133.33)	120.90 [10.26] (117.09; 124.71)	η^2=0.11
Follow-up	123.94 [25.27] (114.56; 133.32)	120.75 [10.32] (116.92; 124.58)	
Quadriceps strength (kg)			
Baseline	268.43 [76.60] (240.01; 296.86)	271.43 [24.75] (262.24; 280.61)	F=4.04; P=0.024
Post-treatment	280.83 [77.20] (252.18; 309.48)	271.33 [26.26] (261.59; 281.08)	η^2=0.04
Follow-up	281.76 [79.81] (252.14; 311.38)	271.52 [26.15] (261.82; 281.23)	
Hamstring strength (kg)			
Baseline	255.70 [61.65] (232.83; 278.58)	254.62 [24.90] (245.38; 263.86)	F=2.54; P=0.08
Post-treatment	263.56 [64.18] (239.74; 287.38)	253.92 [25.11] (2.44.60; 263.24)	η^2=0.02
Follow-up	260.91 [60.44] (238.48; 283.34)	254.28 [25.04] (244.98; 263.57)	

SD: standard deviation; 99% CI: 99% confidence interval; η^2: eta squared.
*P<0.01 with a 99% confidence interval was considered statistically significant.

TABLE III.—*Pairwise comparison analysis of the study.*

Variables	T1-T0	T2-T1	T2-T0
	MD (99% CI)	MD (99% CI)	MD (99% CI)
Joint pain	-0.20 (-0.33; -0.07)*	0.01 (-0.09; 0.12)	-0.21 (-0.36; -0.06)*
Frequency of hemarthrosis	-0.32 (-0.49; -0.15)*	-0.11 (-0.25; 0.02)	-0.21 (-0.42; -0.00)*
Range of motion	0.27 (-0.15; 0.71)	0.14 (-0.22; 0.51)	0.13 (-0.27; 0.54)
Quadriceps strength	6.15 (-0.69; 12.99)	0.56 (-8.63; 9.75)	6.71 (-0.61; 14.04)
Hamstring strength	3.57 (-1.87; 9.02)	-1.14 (-7.26; 4.97)	2.43 (-3.32; 8.19)

MD: mean differences; 99% CI: 99% confidence interval; T1-T0: outcome measures for post-treatment to baseline assessments; T2-T1: outcome measures for follow-up to post-treatment assessments; T2-T0: outcome measures for follow-up to baseline assessments.
*P<0.01 with a 99% confidence interval was considered statistically significant.

TABLE IV.—*Minimum detectable change in the study variables.*

Variables	$ICC_{2,1}$ (SD_{dif})	SEM	MDC	MDC_p
Joint pain	0.97 (0.0.12)	0.02	0.52	Experimental group: 28.84% Control group: 9.61%
Range of motion	0.96 (1.71)	0.34	2.13	Experimental group: 30.76% Control group: 5.76%
Quadriceps strength	0.83 (9.95)	4.10	7.36	Experimental group: 40.38% Control group: 5.76%
Hamstring strength	0.81 (12.77)	5.46	8.49	Experimental group: 42.30% Control group: 1.92%

$ICC_{2,1}$: two-way random intraclass correlation coefficient; SD_{dif}: standard error of the difference in the inter-rater evaluation; SEM: standard error of measurement; MDC: minimum detectable change; MDC_p: proportion of minimal detectable change.

Range of motion

There were statistically significant intergroup differences (P<0.001) in the range of motion of the knee (F[2;204]=13.58). In the pairwise comparison analysis, there were no significant changes. Equal or greater changes in the range of motion after the intervention was reported for 30.76% of the patients in the experimental group.

Muscle strength

There were no statistically significant differences (P>0.01) in the quadriceps (F[1.75; 178.70]=4.04) and hamstring strength (F[2;204]=2.54). There were no significant differences in the pairwise comparison analysis. More than 40% of the patients showed greater changes in quadriceps (MDC=7.36) and hamstring (MDC=8.49) strength.

Discussion

The aim of this study was to evaluate the safety and efficacy of a self-induced myofascial release program using a foam roller in patients with hemophilic knee arthropathy. Improvements in frequency of knee joint bleeding, pain intensity and range of motion were observed after the intervention.

A recent cohort study[19] has shown the safety of myofascial self-release with foam rolling in patients with hemophilic knee arthropathy. This may be explained by the lower mechanical pressure exerted on the joint since foam rolling releases tension in the fascia. Among the neurophysiological effects described with the use of the foam roller, it has been noted that the pressure it causes can relax muscle tissue, reducing local and surrounding pain. This effect is produced through the afferent inputs of the central nervous system (from the Golgi tendon reflexes). In this way the activity rate of the motor unit can be reduced, causing a subsequent relaxation of the muscle. Likewise, the muscle relaxation effect capable of inducing the changes observed in this study may be due to the action of mechanoreceptors and nociceptors, by stimulation of the nervous system or by inhibition of the H reflex.[16]

Chronic pain, related to the loss of functionality, is one of the variables having most impact on the quality of life of patients with hemophilic arthropathy.[35] Foam rolling has shown its effectiveness in improving the pressure pain threshold in the quadriceps muscles[36] in healthy subjects. The improvement reported in our study in terms of reduced intensity of joint pain perceived by the patients treated was maintained after the follow-up period. Such improved perception of chronic pain may be due to the restoration of soft tissue extensibility after the intervention.[37, 38] Similarly, increased blood flow that helps to remove toxins and blocking of the nociceptive stimulation by activating receptors in the skin[18] may favor the effect on the pain intensity of patients.

Limited range of motion is characteristic of hemophilic arthropathy.[39] Foam rolling on the quadriceps muscle on a daily basis can improve the knee range of motion in people without joint damage.[40, 41] In our study we found significant differences in the range of motion of the knee both after the intervention and after 10 weeks of follow-up. Although the intra-articular limitation due to the smaller joint space does not vary, the increased joint mobility observed in our study may be due to the thixotropic property of the tissues. Thanks to this property, the pressure of the roller can reduce the myofascial restrictions causing an elongation of the tissues of the affected area thereby improving the increased joint range.[16]

As a consequence of a degenerative process, the affected joint and related muscles are underused. On the other hand, the fibrosis that develops subsequent to bleeding episodes in the muscles favors the onset of muscle atrophy.[42] Periarticular muscle atrophy is one of the main characteristics in hemophilic arthropathy.[43] Although our study reports significant changes in the quadriceps strength of treated patients, no differences were found with respect to the control group. A number of authors[44, 45] have observed how foam roller-based myofascial self-release exercises can help to preserve muscle strength. The improvement of late-onset muscle pain and its influence on factors such as swelling, and nociceptor activation can improve natural muscle sequencing and agonist-antagonist coordination. Fonta *et al.*[46] reported how a single 7-minute session of myofascial self-release foam rolling in healthy and active patients can improve the strength of the trunk extensor muscles. However, in patients with hemophilia we found no changes after the intervention, which may be due to muscle inhibition as a result of repeated hemarthroses and associated fibrosis.

The intervention carried out in this study is easily replicable in routine clinical practice due to the low cost of the material and the implementation of an easy protocol. Evaluating the frequency of hemarthrosis as the main variable is fundamental for the suitability of this technique for patients with hemophilia.

Limitations of the study

This study presents limitations that must be considered. Among the limitations of the study, we must highlight the impossibility of performing ultrasound evaluations that would rule out microbleeds during the intervention. The absence of anthropometric evaluations is another limitation that prevents detecting possible changes in variables such as muscle volume. Finally, the intake of analgesic drugs by the patients has not been recorded, preventing the correlation of their possible effect on the results.

Conclusions

A protocol based on self-induced myofascial release, along with a therapeutic regimen prescribed by the hemophilic patient's hematologist, can lead to changes in the frequency of hemarthrosis. Following a daily protocol of myofascial self-release exercises may decrease the intensity of pain in patients with hemophilic knee arthropathy. Daily myofascial self-release exercises at home can improve knee range of motion in people with hemophilia and knee arthropathy. Self-induced myofascial release can produce a clinically relevant change in range of motion and muscle strength. The results of this single-blind randomized clinical trial, despite the methodological quality of the study, should be considered based on the limitations listed in the manuscript.

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Conflicts of interest
The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Funding
This research was funded by a grant from Baxalta GmbH, now part of the Takeda Company Group (N. IIR-ES-002614).

Authors' contributions
Elena Donoso-Úbeda, Raúl Pérez-Llanes, Javier Meroño-Gallut, Roberto Ucero-Lozano and Rubén Cuesta-Barriuso contributed equally to the manuscript, Elena Donoso-Úbeda, Javier Meroño-Gallut, Roberto Ucero-Lozano and Rubén Cuesta-Barriuso have given substantial contributions to study conception and design, Roberto Ucero-Lozano and Rubén Cuesta-Barriuso to data acquisition, analysis and interpretation, Elena Donoso-Úbeda, Raúl Pérez-Llanes, Javier Meroño-Gallut, Roberto Ucero-Lozano and Rubén Cuesta-Barriuso to manuscript writing, Elena Donoso-Úbeda to manuscript critical revision. All authors read and approved the final version of the manuscript.

Acknowledgements
The authors acknowledge the Spanish Federation of Hemophilia and the Association of Hemophilia of Andalucía, Bilbao, Burgos, Galicia, Madrid, Murcia, and Valladolid for recruiting sample subjects.

History
Article first published online: October 23, 2023. – Manuscript accepted: October 2, 2023. - Manuscript revised: September 5, 2023. - Manuscript received: February 24, 2023.