Post-Isometric Relaxation for Management of Hemophilic Arthropathy-A Quasi-Experimental Study

Abstract

Aims: Hemophilic arthropathy (HA) is the leading cause of morbidity in persons with severe hemophilia. Post Isometric Relaxation (PIR), a form of muscle energy technique (MET) works on the principle of autogenic inhibition to improve the joint range and muscle strength. No previous reports document their use in HA. Therefore, this study aimed to prospectively compare the effects of PIR combined with conventional physical therapy versus conventional physical therapy alone, in persons with HA.

Materials & Methods: This single-center quasi-experimental study was conducted at a tertiary care center in South India. 50 eligible individuals with knee HA consented to participate. All 50 participants received conventional physical therapy. Of these, 25 received PIR intervention forming the experimental group. The sessions were given thrice a week for 5 consecutive weeks.

Findings: Forty-two out of the 50 who completed the 5-week intervention were included in the analysis. The experimental group demonstrated significant improvement in knee flexion (MD=-18.67±5.66; 95% CI: -24.33, -13.01) and extension (MD=-4.82±1.96; 95% CI: 2.86, 6.78) range of motion (ROM), muscle strength (extensors: MD=-9.93±4.40; 95% CI: -10.12, -1.82; Flexors: MD=-7.83±3.16, 95% CI: -9.25, -1.09), joint health (MD=10.37±4.21; 95% CI: 6.16, 14.58), and joint function (MD=-4.81±1.43; 95% CI: -6.24, -3.38) compared to the control group (p-value<0.05). Nevertheless, both groups significantly improved when compared to their baseline outcomes. (p-value=0.0001).

Conclusion: PIR intervention may improve knee ROM, strength, joint health, and joint function when combined with conventional physical therapy for individuals with HA.

Keywords

Hemophilia A [https://www.ncbi.nlm.nih.gov/mesh/68006467];
Joint Diseases [https://www.ncbi.nlm.nih.gov/mesh/68007592];
Physical Therapy Modalities [https://www.ncbi.nlm.nih.gov/mesh/68026741];
Muscle Relaxation [https://www.ncbi.nlm.nih.gov/mesh/68009126];
Range of Motion, Articular [https://www.ncbi.nlm.nih.gov/mesh/68016059];
Functional Status [https://www.ncbi.nlm.nih.gov/mesh/2052133]

Introduction

Hemophilia is an X-linked inherited disorder affecting around 400,000 people globally, characterized by deficiency of coagulation factors [1]. Hemophilia A, linked to factor VIII, occurs in about 1 in 5,000 male births, while hemophilia B, linked to factor IX, occurs in about 1 in 30,000 [2]. It is classified into three categories: Severe (factor activity level: <1 IU/dl or <1%), moderate (1%-5%), and mild (5%-40%) [3].

In individuals with hemophilia (PWH), bleeding into the joints accounts for 80% to 90% of all bleeding episodes. This is especially true for those with severe hemophilia, where bleeding can occur spontaneously or after minimal stress or trauma [4, 5]. The knee joint is the most commonly affected area due to its large synovial membrane and the significant rotational forces involved [6].

Recurrent bleeding in the knee joint often leads to chronic hemophilic arthropathy (HA), characterized by pain, swelling, soft tissue contractures, and damage to cartilage and bone [7-9]. This cartilage destruction results from direct exposure to blood and inflammation in the synovium. Even brief exposure can cause lasting damage [10, 11]. The inflammation and synovial hypertrophy in HA resemble those in rheumatoid arthritis, while the degeneration of hyaline cartilage is similar to osteoarthritis. These overlapping processes can lead to progressive joint destruction [10, 12].

Most management recommendations for HA focus on pharmacological treatment and factor replacement therapy. Despite improved treatments to prevent recurrent joint bleeding, blood-induced HA remains a major source of morbidity in hemophilia, significantly affecting the quality of life [14]. The knees are the most commonly affected joints (45%) in patients without prophylactic treatment [6, 13]. In severe hemophilia, the first hemarthrosis typically occurs around age 2, and if untreated, can lead to hemophilic arthropathy by age 20 [15].

Non-pharmacological management includes a variety of physical therapy interventions, such as isometric and isotonic exercises, strength and balance training, cycling, treadmill walking, hydrotherapy, manual therapy techniques, proprioceptive training, and physical activity [16-28]. These approaches have shown a potential to improve the quality of life in PWH by enhancing mobility and function. However, the limited number of studies and diverse outcomes prevent confirmation of their efficacy. Therefore, further robust research is needed to evaluate rehabilitation and physiotherapy in managing chronic HA in PWH [29].

Muscle energy technique (MET) is a manual therapy that has been shown to increase the range of motion (ROM) and improve function in many joints. Post Isometric Relaxation (PIR) is a type of MET that works on the principle of autogenic inhibition to improve the joint range and muscle strength. It involves putting increased tension on the muscle fibers by asking the patient to contract against the resistance of the therapist, activating the Golgi tendon organ, which leads to reflex inhibition and muscle relaxation, allowing for effective passive stretching [30, 31].

PIR is used in managing various musculoskeletal conditions based on the principles of restoring biomechanics and minimizing movement restriction and pain [30-32]. A few studies demonstrate the effectiveness of MET on other musculoskeletal conditions either as a stand-alone intervention or in combination with other therapeutic exercises with a positive therapeutic impact on joint mobility, muscle strength, and pain reduction, although they lack strong methodology [33]. As far as our literature search goes, no studies describe the application of PIR in HA, although it is extensively used for other musculoskeletal populations. Thus, in individuals with HA, this study aimed to prospectively assess the efficacy of PIR in addition to conventional physical therapy versus conventional physical therapy alone.

Materials and Methods

Study design

This study was a quasi-experimental study done at a single center. Approval for this study was obtained from the Institutional Ethics Committee, Krupanidhi College of Physiotherapy (EC-MPT/23/PHY/001), South India.

Study setting and participants

Persons with severe hemophilia A or B with HA of the knee joint, who were registered in the Hemophilia treatment care center of the Hemophilia Society in South India, were assessed for eligibility, following which written consent was obtained by the principal investigator in their regional language. To be eligible for inclusion, the participants had to be diagnosed with HA of the unilateral knee joint of any duration and should be between 18 and 40 years old. Participants who had recent joint or muscle bleeds within 1 month in the lower limbs, knee surgeries, FVIII or FIX inhibitors, neurological conditions, or cognitive impairments affecting functional levels, and those on regular physical therapy within three months before the treatment commenced were excluded from the study.

Group allocation and blinding

The eligible participants were assigned to either the control (n=25) or experimental (n=25) group by an independent researcher using a convenient sampling method, at the out-patient unit in physiotherapy. The control group received conventional physical therapy, and the experimental group received PIR intervention in addition to conventional physical therapy. A baseline assessment of demographic data, health history, and outcomes including knee ROM, muscle strength, joint health, and function, was done by an outcome assessor blinded to the group allocation or the treatment received in both groups. A detailed diagrammatic flow chart of the study is shown in Figure 1.

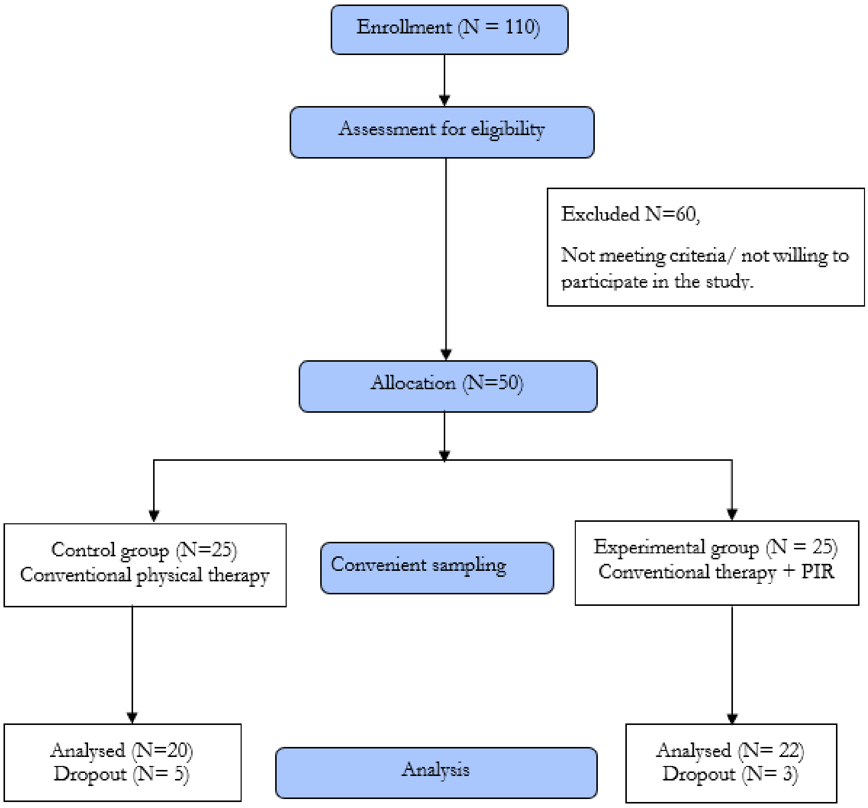

Figure 1. Consort flow diagram of participants

Outcome measures

The outcomes were measured before and after the physical therapy intervention for the control and experimental groups. The knee ROM was assessed using a standard goniometer which is widely used in clinical practice with good intra-tester and inter-tester reliability [34]. The strength of the knee extensor and flexor muscles was quantified using the Lafayette Hand-Held Dynamometer (HHD), a valid assessment tool for objectively quantifying muscle strength with high inter- and intra-rater reliability [35]. The joint health was measured using the Hemophilia Joint Health Score (HJHS), a validated scale for physical examination of joint health in hemophilia, with excellent inter-observer and test-retest reliability [36]. The total HJHS score was analyzed in this study. The Functional Independence Score in Hemophilia (FISH) was used to assess their independence in functional activities; A reliable tool, developed and validated in a group of patients with significant HA [37].

Intervention

All 50 selected participants received conventional physical therapy for 30 minutes, three times a week for five consecutive weeks. In addition to this standard therapy, 25 out of the 50 participants were selected using convenient sampling. They received PIR intervention for 15 minutes, three times a week for five consecutive weeks, alongside the conventional therapy. All interventions were given without prophylactic factor replacement therapy.

Conventional therapy

All 50 participants, the control (25) and experimental group (25) received conventional therapy. Graded strengthening exercises were given to the hip, knee, and ankle muscles. The exercise progressed from active free movements to resisted exercise; Resistance using weight cuffs was gradually increased every week; Starting from 10 repetitions and gradually increasing the repetitions to 20. Active stretching of the hamstrings, hip flexors, and calf muscles was given in non-weight bearing position and the duration of stretch was increased as tolerated by the patient without inducing a joint bleed. Balance and proprioceptive training were given in weight-bearing positions with or without an assistive device as required. The exercise intensity was tailored according to the participants' joint bleed history and pain [38].

PIR intervention

Of the 50 participants, 25 who belonged to the experimental group received PIR for the hamstrings and quadriceps muscles to improve knee extension and flexion ROM respectively.

PIR for hamstring muscle (knee extension): In the supine position, the affected limb of the patient was lifted to assess the limitation in the knee extension range. At the point of restriction, the patient was asked to press the leg downward into flexion using 10% of his maximal effort while the therapist resisted the movement (Figure 2). The patient was asked to hold for 7-8 seconds while contracting the hamstring muscle isometrically and then to relax the muscle completely. The therapist moved the limb up to a new barrier while the patient relaxed and repeated the same technique. This was repeated 10 times.

Figure 2. Post-isometric relaxation applied for hamstring muscles

PIR for quadriceps muscle (knee flexion): The patient was positioned in prone lying. The affected limb was passively bent at the knee joint, by the therapist to assess the knee flexion limitation. At the point of tissue restriction, the patient was instructed to press the limb into extension against the therapist's resistance using 10% of their strength to contract isometrically (Figure 3). The patient was asked to hold for 7-8 seconds while contracting the quadriceps muscle isometrically and then to relax the muscle completely. While the patient relaxed, the therapist moved the limb into flexion to a new barrier and repeated the same technique. This was repeated 10 times.


Figure 3. Post-isometric relaxation applied for quadriceps muscle

Statistical analysis
IBM SPSS version 29.0 for Windows was used to analyze the data. A one-sample t-test was used to compare the average age of the groups and to analyze pre- and post-test measurements of knee flexion, knee extension, quadriceps strength, and hamstring strength. Within each group, paired t-tests were utilized to assess changes over time. The Wilcoxon test was employed to compare the ordinal HJHS and FISH scores before and after the tests between the groups. Group results were contrasted using the Mann-Whitney U test. Pearson correlation analysis was used to compare the ROM, including flexion and extension, with dynamometry measurements for quadriceps and hamstring strength. The correlation between HJHS and FISH scores was assessed using Spearman's correlation. The effect size was calculated using the mean difference, and the 95% confidence interval was determined for the outcomes. These statistical tests evaluated the significance of the variables in the current study and their relationships.

Findings
Patients
Out of a total of 110 PWH with HA, who were registered in the Hemophilia Treatment Care Center, 50 eligible individuals were selected and assigned to either the control (n=25) or experimental (n=25) groups, using convenient sampling. The data of 42 participants who completed 5 weeks of treatment sessions were included in the study and their outcomes were analyzed. There was a total of 8 dropouts (5, control and 3, experimental group) due to personal reasons (N=5) and non-compliance to treatment protocol (N=3). The patients' demographics and baseline characteristics and outcomes were similar at baseline in both groups (p-value>0.05; Table 1). This ensured the homogeneity of the participants in the control and experimental groups. All the participants were on episodic factor replacement therapy.

Table 1. Baseline characteristics of participants with HA in control and experimental groups

Patient characteristics	Control (N=20)	Experimental (N=22)	p-value
Age (years)	27.40±4.53	30.36±5.26	0.06
Type of hemophilia			-
Hemophilia A (%)	19 (95)	22 (100)	
Hemophilia B (%)	1 (5)	-	
Prophylaxis	None	None	-
Flexion ROM	104.55±9.49	101.42±10.69	0.32
Extension ROM	10.00±4.51	10.27±3.61	0.83
Quadriceps strength	48.38±8.34	46.72±9.31	0.55

Hamstring strength	47.43±7.56	46.96±4.92	0.85
HJHS (v 2.1)	47.85±6.53	47.23±7.26	0.61
FISH	22.15±3.03	21.55±2.65	0.42

* Significant (p-value<0.05); ROM: Range of motion; HJHS (v 2.1): Hemophilia Joint Health Score (version 2.1); FISH: Functional Independence Score in Hemophilia. Categorical variables are expressed as numbers (%) and continuous variables as mean and standard deviation.

The results of the physical therapy intervention were compared between their baseline findings and the final outcome following 5 weeks of interventions within the two groups (Table 2). Both the control and experimental groups showed significant improvements in joint range of motion (ROM), muscle strength, and overall joint health and function (p-value=0.001). This indicates an excellent response of the joints to physical therapy in both groups.

Table 2. Comparison of outcomes before and after treatment within the control and experimental group

Outcome measures	**Control (N=20)**					**Experimental (N=22)**				
	Initial	**Final**	**Mean difference**	**CI (95%)**	**p-value**	**Initial**	**Final**	**Mean difference**	**CI (95%)**	**p-value**
Flexion ROM	104.55±9.49	114.60±6.87	-10.05±5.13	-15.18, -4.92	0.001*	101.42±10.69	120.09±8.30	-18.67±5.66	-24.33, -13.01	0.001*
Extension ROM	10.00±4.51	7.75±4.07	2.25±2.66	-0.41, 4.91	0.001*	10.27±3.61	5.45±2.99	4.82±1.96	2.86, 6.78	0.001*
Quadriceps strength	48.38±8.34	50.68±8.13	-2.30±5.10	-7.4, 2.8	0.001*	46.72±9.31	56.65±4.92	-9.93±4.40	-4.33, -5.50	0.001*
Hamstring strength	47.43±7.56	49.62±7.30	-2.19±4.61	-6.8, 2.42	0.001*	46.96±4.92	54.79±5.75	-7.83±3.16	-10.99, -4.67	0.001*
HJHS	47.85±6.53	42.55±6.46	5.30±4.02	1.28, 9.32	0.001*	47.23±7.26	36.86±6.99	10.37±4.21	6.16, 14.58	0.001*
FISH	22.15±3.03	23.60±2.52	-1.45±1.73	-3.18, 0.28	0.001*	21.55±2.65	26.36±2.15	-4.81±1.43	-6.24, -3.38	0.001*

* Significant (p-value<0.05); ROM: Range of motion; HJHS (v 2.1): Hemophilia Joint Health Score (version 2.1); FISH: Functional Independence Score in Hemophilia.

The outcomes of physical therapy interventions were compared between the control and experimental groups (Table 3). Baseline values for joint range, muscle strength, HJHS, and FISH for both groups were similar (p-value>0.05). Individuals who received Proprioceptive Neuromuscular Facilitation (PNF) along with conventional therapy demonstrated significant improvement in knee flexion (MD=-18.67±5.66; 95% CI: -24.33, -13.01) and extension (MD=-4.82±1.96; 95% CI: 2.86, 6.78) range, muscle strength (extensors: MD=-9.93±4.40; 95% CI: -10.12, -1.82; Flexors: MD=-7.83±3.16, 95% CI: -9.25, -1.09), joint health (MD=10.37±4.21; 95% CI: 6.16, 14.58), and joint function (MD=-4.81±1.43; 95% CI: -6.24, -3.38; Table 2) compared to those in the control group (p-value<0.05). This improvement can be attributed to the inclusion of the PNF technique in the experimental group (Table 3).

Table 3. Comparison of outcomes before and after 5 weeks of intervention between the control and experimental group

Outcome measures	**Initial (before therapy)**				**Final (after 5 weeks of therapy)**			
	Control (N=20)	**Experimental (N=22)**	**CI (95%)**	**p-value**	**Control (N=20)**	**Experimental (N=22)**	**CI (95%)**	**p-value**
Flexion ROM	104.55±9.49	101.42±10.69	-3.20, 9.46	0.322	114.60±6.87	120.09±8.30	-10.27, -0.71	0.026*
Extension ROM	10.00±4.51	10.27±3.61	-2.81, 2.27	0.826	7.75±4.07	5.45±2.99	0.09, 4.51	0.040*
Quadriceps strength	48.38±8.34	46.72±9.31	-3.87, 7.19	0.549	50.68±8.13	56.65±4.92	-10.12, -1.82	0.045*
Hamstring strength	47.43±7.56	46.96±4.92	-3.47, 4.41	0.853	49.62±7.30	54.79±5.75	-9.25, -1.09	0.014*
HJHS	47.85±6.53	47.23±7.26	-3.70, 4.94	0.614	42.55±6.46	36.86±6.99	1.48, 9.90	0.013*
FISH	22.15±3.03	21.55±2.65	-1.71, 2.37	0.424	23.60±2.52	26.36±2.15	-4.22, 1.30	0.020*

* Significant (p-value<0.05); ROM: Range of motion; HJHS (v 2.1): Hemophilia Joint Health Score (version 2.1); FISH: Functional Independence Score in Hemophilia.

Table 4 shows the correlation between the outcome variables. The correlation between knee range of motion (ROM) and knee muscle strength was found to be weakly positive to moderately negative (Table 4). This suggests that as the range improves, muscle strength may increase. Flexion and extension range of motion (ROM) had a moderate negative correlation, indicating that as knee extension improves, flexion decreases. There was a strong positive correlation found between quadriceps and hamstring strength. This correlation may be attributed to the irradiation of muscles, where the strong contraction of one muscle group can activate nearby muscles, resulting in increased overall force production. A weak negative correlation was observed between joint health and function. This discrepancy arises because the HJHS score uses a negative scoring system, while the FISH utilizes a positive scale. However, this correlation was not statistically significant (Table 4).

Table 4. Correlation between outcome variables

Variables		Pearson correlation coefficient (r)	p-value
Flexion ROM	Quadriceps strength	0.332	0.032
	Hamstring strength	0.294	0.059
Extension ROM	Quadriceps strength	-0.372	0.015
	Hamstring strength	-0.436	0.004
Flexion ROM	Extension ROM	-0.435	0.004
Quadriceps strength	Hamstring strength	0.943	0.0001
HJHS	FISH	-0.087	0.582

* Significant (p-value<0.05); ROM: Range of motion; HJHS (v 2.1): Hemophilia Joint Health Score (version 2.1); FISH: Functional Independence Score in Hemophilia.

Discussion

This quasi-experimental study aimed to prospectively compare the effects of PIR combined with conventional physical therapy versus conventional physical therapy alone, in persons with HA.

The mean ages of PWH with HA in the experimental and control groups at the start of treatment were 30.36±5.26, and 27.40±4.53 years, respectively (Table 1). This is consistent with other research showing that HA usually begins in early childhood and advances before age thirty [39]. Our study participants were all on episodic factor replacement therapy, which could have contributed to their early HA. Literature suggests that in the absence of prophylactic factor replacement therapy, individuals are likely to develop HA by the age of 20 [15]. The majority of them had severe hemophilia A (Table 1), which is consistent with earlier findings that hemophilia A is more common than hemophilia B [2]. The patient characteristics were homogeneous at baseline in both groups (p-value>0.05; Table 1).

We observed a significant improvement in outcomes in both groups after 5 weeks of intervention (Table 2). Similar to the experimental group that received both conventional therapy and PIR intervention, the control group, which received conventional therapy, showed a significant improvement in their range of motion, muscle strength, and overall joint health and function (p-value<0.05; Table 2).

This finding is not surprising, as physical therapy has been shown to improve outcomes for PWH who have multiple joints affected by arthropathies [29]. In our study, we provided graded strengthening exercises using resistance, active stretching for tight muscles, balance training, and proprioceptive training. These activities were tailored according to each participant's initial assessment to prevent the risk of inducing a joint bleed [38].

Resistance training has shown significant improvements in various outcomes in PWH, according to existing literature [16, 23, 24, 29, 40]. A study comparing the effects of a progressive resistance training program with other exercise modalities on joint function in young individuals with hemophilia found that all groups that included resistance training experienced significant improvements in joint function [23]. Furthermore, some studies have documented that while improvements can occur with electrotherapy modalities, it is clear that exercise may enhance these effects [24]. According to a systematic review of the impact of exercise on musculoskeletal function and pain, it was concluded that supervised programs using resistance training, or balancing training may help improve muscle strength, range of motion, and pain in PWH with HA [16, 17]. Besides, it is reported that physical therapy incorporating, strength training, balance exercises, and proprioception, significantly improves joint range of motion, position sense, static and dynamic balance, and pain in individuals with chronic arthropathy, according to a comprehensive review [40].

In our study, both the control group and the experimental groups received traditional interventions, which may explain the improved outcomes observed in both groups (Table 2). However, individuals who received PIR along with conventional therapy showed a significantly greater increase in their range of motion, muscle strength, and overall joint health and function compared to those in the control group (p-value<0.05; Table 3). When comparing the mean difference between the pre- and post-outcomes of the experimental to the control group, the experimental group showed a higher mean difference than the control group (p-value<0.05; Table 2).

The improvements in knee range of motion (ROM) observed in the experimental group that received PIR intervention may be due to the relaxation and lengthening of muscles that occur following an isometric contraction, a phenomenon known as autogenic inhibition. It is believed that after an isometric contraction, reflexive inhibition and relaxation of the muscle enable the clinician to perform a passive stretch because the muscle is in a refractory state [30, 31].

Our findings align with previous studies demonstrating that PIR is effective in improving the outcomes in joint arthropathies [30-32]. Additionally, earlier studies have demonstrated that MET, including PIR, either as a stand-alone intervention or along with other therapeutic exercises has a positive impact on joint mobility, muscle strength, and pain reduction [33].

There were no worsening of outcomes or adverse events that were reported by any of the individuals in both groups. HA is a major morbidity of hemophilia with a considerable impact on the quality of life in PWH [14], with the knee affected the most, particularly in persons who do not have access for prophylactic factor replacement therapy [6, 13]. The current study, along with previous research, suggests that PIR when combined with conventional physical therapy interventions, may be effective for improving outcomes in the management of HA in PWH. However, the theoretical rationale for this clinical finding is not established based on this evidence alone.

Although this was a quasi-experimental study, some measures were implemented to reduce bias, including the use of an independent researcher for allocating the individuals to the intervention groups, blinding the outcome assessor and ensuring comparable baseline characteristics among participants. Despite these points, several limitations were identified in our study. Firstly, the lack of randomization may have introduced a selection bias, as we could not deny treatment to participants with hemophilia who wanted PIR intervention. Secondly, the use of convenient sampling methods for participant assignment may reduce the external validity of the findings. Additionally, while only the outcome assessor was blinded, neither the therapists nor the participants were blinded, which could lead to potential performance bias. However, due to the nature of the intervention, blinding the study subjects and therapists was not feasible. Other limitations included the absence of a placebo or non-treatment group and the absence of long-term follow-up.

It is essential to conduct robust, well-designed randomized clinical studies to evaluate the effects of physical therapy including PIR intervention, in managing chronic HA in PWH. These studies should involve larger participant groups and include extended follow-up periods to assess long-term effectiveness. Currently, it is unclear whether the benefits of physical therapy intervention persist over time. Despite these limitations, this is the first study to report the effect of PIR intervention in persons with severe hemophilia for the management of knee HA.

Conclusion

PIR may be a useful and appropriate intervention for managing hemophilia-associated arthropathy in individuals with hemophilia. However, further clinical evaluation of this treatment is necessary through well-designed studies. Additionally, there should be a greater effort to optimize the technique of PIR and to understand the underlying reasons for the benefits experienced by patients.