

Electromyographic and Safety Comparisons of Common Lower Limb Rehabilitation Exercises for People With Hemophilia

Calatayud, Joaquín; Pérez-Alenda, Sofía; Carrasco, Juan J; Escriche-Escuder, Adrián; Cruz-Montecinos, Carlos; Andersen, Lars L; Bonanad, Santiago; Querol, Felipe; Casaña, José

Published in:
Physical Therapy

DOI (link to publication from Publisher):
[10.1093/ptj/pzz146](https://doi.org/10.1093/ptj/pzz146)

Publication date:
2020

Document Version
Accepted author manuscript, peer reviewed version

[Link to publication from Aalborg University](#)

Citation for published version (APA):

Calatayud, J., Pérez-Alenda, S., Carrasco, J. J., Escriche-Escuder, A., Cruz-Montecinos, C., Andersen, L. L., Bonanad, S., Querol, F., & Casaña, J. (2020). Electromyographic and Safety Comparisons of Common Lower Limb Rehabilitation Exercises for People With Hemophilia. *Physical Therapy*, 100(1), 116-126.
<https://doi.org/10.1093/ptj/pzz146>

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal -

Take down policy

If you believe that this document breaches copyright please contact us at vbn@aub.aau.dk providing details, and we will remove access to the work immediately and investigate your claim.

TITLE: Electromyographic and Safety Comparisons of Common Lower Limb Rehabilitation Exercises for People With Hemophilia

RUNNING HEAD: Lower Limb Exercises in Hemophilia

TOC CATEGORY: Musculoskeletal

ARTICLE TYPE: Original Research

AUTHOR BYLINE: Joaquín Calatayud, Sofía Pérez-Alenda, Juan J. Carrasco, Adrián Escriche-Escuder, Carlos Cruz-Montecinos, Lars L. Andersen, Santiago Bonanad, Felipe Querol, José Casaña

AUTHOR INFORMATION:

J. Calatayud, PhD, Department of Physiotherapy, Exercise Intervention for Health Research Group (EXINH-RG), University of Valencia, Valencia, Spain; and National Research Centre for the Working Environment, Copenhagen, Denmark.

S. Pérez-Alenda, PT, PhD, Haemostasis and Thrombosis Unit, University and Polytechnic Hospital La Fe, Valencia, Spain; and Department of Physiotherapy, Physiotherapy in Motion Multispeciality Research Group (PTinMOTION), University of Valencia, c/ Gascó Oliag 5, CP 46010, Valencia, Spain. Address all correspondence to Dr Pérez-Alenda at: sofia.perez-alenda@uv.es.

J.J. Carrasco, MSc, Department of Physiotherapy, Physiotherapy in Motion Multispeciality Research Group (PTinMOTION), University of Valencia; and Intelligent Data Analysis Laboratory, University of Valencia.

A. Escriche-Escuder, PT, MSc, Department of Physiotherapy, University of Malaga, Malaga, Spain.

C. Cruz-Montecinos, PT, MSc, Department of Physiotherapy, Physiotherapy in Motion Multispeciality Research Group (PTinMOTION), University of Valencia; Laboratory of Clinical Biomechanics, Department of Physical Therapy, Faculty of Medicine, University of Chile, Santiago, Chile; and Laboratory of Biomechanics and Kinesiology, San José Hospital, Santiago, Chile.

L.L. Andersen, PhD, National Research Centre for the Working Environment; and Sport Sciences, Department of Health Science and Technology, Aalborg University, Aalborg, Denmark.

S. Bonanad, MD, MSc, Haemostasis and Thrombosis Unit, University and Polytechnic Hospital La Fe.

F. Querol, PT, MD, PhD, Haemostasis and Thrombosis Unit, University and Polytechnic Hospital La Fe; and Department of Physiotherapy, Physiotherapy in Motion Multispeciality Research Group (PTinMOTION), University of Valencia.

J. Casaña, PT, RN, PhD, Department of Physiotherapy, Exercise Intervention for Health Research Group (EXINH-RG), University of Valencia.

KEYWORDS: Ankle, Exercise Therapy, Knee, Hamstring, Quadriceps, EMG

ACCEPTED: April 19, 2019

SUBMITTED: December 4, 2018

Background. Ankles and knees are commonly affected in people with hemophilia and thus are targets for prevention or rehabilitation. However, to our knowledge, no studies have evaluated muscle activity and safety during exercises targeting the lower limbs in people with hemophilia; this lack of information hinders clinical decision-making.

Objective. The aim of this study was to compare the tolerability of, safety of, and muscle activity levels obtained with external resistance (elastic or machine)–based and non–external resistance–based lower limb exercises in people with hemophilia.

Design. This was a cross-sectional study.

Methods. Eleven people who had severe hemophilia and were undergoing prophylactic treatment participated. In a single experimental session, participants performed knee extension and ankle plantar flexion during 3 exercise conditions in random order: elastic band–based resistance (elastic resistance), machine-based resistance (machine resistance), and no external resistance. Exercise intensities for the 2 external resistance–based conditions were matched for perceived exertion. Muscle activity was determined using surface electromyography (EMG) for the rectus femoris, biceps femoris, gastrocnemius lateralis, and tibialis anterior muscles. Participants were asked to rate exercise tolerability according to a scale ranging from “very well tolerated” to “not tolerated” and to report possible adverse effects 24 and 48 hours after the session.

Results. No adverse effects were reported, and exercise tolerability was generally high. In the knee extension exercise, the rectus femoris normalized EMG values during the elastic resistance and machine resistance conditions were similar; 29% to 30% higher

activity was obtained during these conditions than during the non—external resistance condition. In the ankle plantar flexion exercise, the gastrocnemius lateralis normalized EMG value was 34% higher during the machine resistance condition than without external resistance, and the normalized EMG values during the elastic resistance and other conditions were similar.

Limitations. The small sample size and single training session were the primary limitations of this study.

Conclusions. Exercises performed both with elastic bands and with machines at moderate intensity are safe, feasible, and efficient in people with severe hemophilia, providing comparable activity levels in the agonist muscles.

Hemophilia is an inherited bleeding disorder with an average prevalence of approximately 1/10,000 of the population.¹ Arthropathy will be experienced in the second or third decade of life by about 90% of people with severe hemophilia,¹ with ankles and knees being the joints² most commonly affected by proliferative synovitis and cartilage destruction.¹ This progressive joint damage causes pain, reduced range of motion, and reduced muscle cross-sectional area and strength,³ affecting function and quality of life. Even in young people with hemophilia, knee extensor strength⁴ and ankle plantar flexor muscle architecture and strength⁵ are associated with common daily activities such as walking. Thus, strengthening exercise should be a cornerstone of rehabilitation programs,⁶ being even more relevant with aging⁷ and severe arthropathy⁸ due to muscle wasting and strength loss; these issues accelerate loss of functionality, impair walking ability, and increase the risk of falls.⁹

Strength training can be performed with many different types of equipment or resistance, which can result in different training stimuli.¹⁰ These choices should be taken into account in the design of appropriate therapeutic exercise programs. For instance, traditional training machines and elastic bands are 2 typically used equipment with different properties.¹¹ On the one hand, traditional training machines allow easily standardized movement, quantify load, and train with high intensities. On the other hand, machine-based equipment is expensive and not feasible for home-based exercise, making training dependent on special facilities; these factors may negatively affect participation in training. In contrast, elastic resistance bands are relatively inexpensive and portable, allowing exercise to be performed anywhere.

Perhaps even more importantly for people with hemophilia, training with elastic resistance bands—in contrast to heavy weights—may prevent accidents or injuries due to sudden high impact forces. Although elastic resistance bands were used as a complement to free weights in a previous study of people with hemophilia,¹² it is unknown whether elastic resistance bands are feasible, tolerable, and effective alternatives to traditional training machines for activating knee and ankle muscles.

Some studies reported different lower limb muscle activity levels and patterns in comparisons of elastic bands with free weights or machines in adults with and without musculoskeletal pain¹³ and in patients with chronic stroke.¹⁰ However, most previous studies in adults who were healthy reported comparable hamstring muscle activity levels during knee flexion¹⁴ and quadriceps muscle activity levels^{15,16} during knee extension when the exercises were performed with machine-based resistance (machine resistance) and elastic band–based resistance (elastic resistance). However, to our knowledge, no studies have evaluated muscle activity during exercises targeting the lower limbs in people with hemophilia; this fact hinders clinical decision-making about proper therapeutic exercises.

The purpose of the present study was to compare the tolerability of, safety of, and muscle activity levels obtained with external resistance (elastic or machine)–based and non–external resistance–based lower limb exercises in people with hemophilia. We hypothesized that the elastic resistance and machine resistance exercises would result

in similar muscle activity levels in the agonist muscles, with comparable tolerability and without adverse effects in the days following the training session.

[H1] Methods

[H2] Participants

During May to June 2017 at a local hospital (University and Polytechnic Hospital La Fe, Valencia, Spain), patients who were at least 18 years old, diagnosed with severe hemophilia, and undergoing prophylactic treatment were considered candidates for the present study. Exclusion criteria were joint replacement in the previous year, joint or muscle bleeding in the last 3 months, or any medical condition in which exercise is contraindicated. A total of 11 patients who had severe hemophilia and were receiving prophylactic treatment (10 type A; 1 type B) voluntarily participated in the study, which was performed at the University of Valencia (Valencia, Spain) during June 2017. Most of the participants were performing exercise at least once per week when they participated in the study. All participants were informed about the purpose and content of the investigation. Written informed consent was obtained from all individual participants in the study. The study conformed to the Declaration of Helsinki and was approved by the local ethics committee (ref. no. H1461147538087). Data reported in the present study are part of a research project investigating muscle activity during different exercises in people with hemophilia. This article adheres to the STROBE guidelines.¹⁷

[H2] Procedures

The following clinical variables were collected from the medical record: type of hemophilia and severity, prophylaxis regimen (weekly coagulation factor dose), annual bleeding joint rate (ABJR) in lower limbs and degree of hemophilic arthropathy in knees and ankles measured radiologically with the Pettersson score. This score evaluates the different elements of the articular alteration using an additive score of 0 to 13 per joint, with 0 indicating normality and 13 indicating maximum joint alteration.¹⁸ Regarding pharmacokinetics, Bayesian post hoc estimation of individualized pharmacokinetics values (half-life and peak level) was obtained using the Web-Accessible Population Pharmacokinetic Service—Hemophilia (WAPPS-Hemo tool).¹⁹

Each participant took part in 1 experimental session. Several restrictions were imposed on the volunteers: no food, drinks or stimulants (eg, caffeine) to be consumed 2 hours before the sessions and no physical activity more intense than daily activities 24 hours before the exercises. They were recommended to sleep at least 7 to 8 hours the night before data collection. All measurements were made by the same 2 investigators and were conducted in the same facility.

Two days before the experimental session, the participants received a video with the exercises that had to be performed in order to visualize the proper exercise technique.

The participants attended the experimental session 1 to 2 hours after receiving their

routine coagulation factor prophylaxis treatment. In the experimental session, height (determined with a stadiometer; model IP0955 [Invicta Plastics Ltd, Leicester, England]) and body mass (determined with a body composition analyzer; model BF-350 [Tanita, Tokyo, Japan]) were obtained. Degree of hemophilic arthropathy was clinically evaluated in knees and ankles by using the Hemophilia Joint Health Score 2.1. This instrument scores each joint from 0 to 20 points, with higher scores reflecting worse conditions (having a maximum score of 80 points for knees and ankles).²⁰ Subsequently, participants answered a short questionnaire about leisure-time physical activity²¹ and their resistance training experience. Afterward, the electromyography (EMG) protocol started with the preparation of participants' skin, followed by electrode placement, maximum voluntary isometric contraction (MVIC) collection, and performance of exercises.

Hair was removed from the skin overlying the muscles of interest, and the skin was then cleaned by rubbing with cotton wool dipped in alcohol for the subsequent electrode placement. Electrodes were placed according to SENIAM (surface EMG for noninvasive assessment of muscles) recommendations²² on the rectus femoris, biceps femoris, gastrocnemius lateralis, and tibialis anterior muscles on the dominant side of the body, which was determined by asking about the preferred leg used to kick a ball. Specifically, electrodes were placed at 50% of the line from the anterior spina iliaca superior to the superior part of the patella, 50% of the line between the ischial tuberosity and the lateral epicondyle of the tibia, one-third of the line between the

head of the fibula and the heel, and one-third of the line between the tip of the fibula and the tip of the medial malleolus.

Pregelled bipolar silver/silver chloride (Ag/AgCl) surface disk-shape electrodes (Blue Sensor N-00-S; Ambu A/S, Ballerup, Denmark) with an electrode size of 44.8 x 22 mm and a measuring area of 95 mm² were placed with an interelectrode distance of 2 cm. The reference electrode was placed approximately 10 cm away from each muscle, over a body landmark, according to the manufacturer's specifications. Electrodes were connected directly to differential preamplifier cables (preamplifier gain = 305) with an ME6000P8 (Mega Electronics, Ltd, Kuopio, Finland) biosignal conditioner. All signals were acquired at a sampling frequency of 1 kHz with a bandwidth of 8 to 500 Hz to avoid aliasing. The common mode rejection ratio was 110 dB. Before starting each exercise condition, we checked offset values for each channel to ensure that they were within a $\pm 2\text{-}\mu\text{V}$ range of 0 μV . All records of myoelectrical activity (in microvolts) were stored on a hard drive for later analysis.

Prior to performance of the exercise described below, an MVIC with a duration of 5 seconds was performed for each muscle. Participants performed a nonmaximal practice trial to ensure that they understood the task. They were asked to exert progressive contraction for 2 seconds and to maintain 3 seconds of maximal contraction without reaching a pain intensity of >4 of 10 on a numerical pain rating scale. In case of reaching greater pain than 4, an additional practice trial was allowed after resting. One minute of rest was given between each MVIC and verbal

encouragement was provided to motivate all participants to achieve maximal muscle activity. Positions during the MVIC evaluations were based on standardized muscle testing procedures for the rectus femoris, biceps femoris,¹⁶ gastrocnemius lateralis, and tibialis anterior²³ muscles. Specifically, seated knee extension/flexion with a knee angle of 70 degrees and a hip angle of 110 degrees was performed against a fixed resistance for the rectus femoris and biceps femoris muscles, and ankle plantar flexion and dorsal flexion were performed against manual resistance while the participant was seated with knees fully extended and the ankle in a neutral position.

Participants performed 2 exercises: knee extension (Fig. 1) and ankle plantar flexion (Fig. 2) in 3 different conditions (elastic resistance, machine resistance, and no external resistance). All 6 conditions were randomly used for each participant. Knee extension exercises were performed on a seated knee extension machine with back support (F&H Fitness Equipaments, Vila-Real, Spain); either the machine load or the attached elastic resistance was used, the knee flexion angle was 70 degrees, and the hip flexion angle was 110 degrees. In addition, the knee extension machine was also used to perform the non-external resistance condition. The non-external resistance condition consisted of performing the same action, with the same exercise technique, but with no additional weight or elastic resistance, using only body weight as load.

The ankle plantar flexion with the elastic resistance was performed in a seated knee extension/flexion machine. For this condition, the participants were seated with knees fully extended and the band looped around 1 foot while the extremes were attached

to the machine. In addition, this machine also served to perform the ankle plantar flexion without external resistance. The machine-based ankle plantar flexion was performed in a leg press machine (F&H Fitness Equipaments), with fully extended knees, pressing the load with 1 foot. The exercises had to be performed with the participant's available range of motion, as close as possible to the original exercise technique. Participants were asked to use minimal lower body and trunk movement, and to perform the exercise without sudden jerks or accelerations. A metronome was used to standardize movement velocity at a 1.5-second rate for concentric and a 1.5-second rate for eccentric actions, and feedback was provided to the participants if any deviance was observed. A trial was discarded and repeated if participants were unable to perform the exercise properly.

Before starting each exercise, we aimed to match relative perceived intensity—ie, not the same absolute load—across conditions performed with external resistance.

Participants performed 6 light intensity repetitions to warm-up and then 2-3 additional sets of 3 repetitions (with EMG recording), with 1-min rest between sets until they rated a 6 on the Borg CR10 Scale. This intensity was selected as it corresponds to a weight allowing for approximately 12 repetitions,²⁴ which is considered moderate intensity.²⁵ Only the set where the participants reached the desired intensity was stored for later EMG analysis. Previous studies found a moderate to very strong association among perceived loading with the Borg CR10 Scale, actual loading, and normalized EMG amplitude of the prime muscles when using the same exercise performed with elastic bands or weights.^{26,27}

To achieve adequate exercise intensity during the elastic resistance conditions, the elastic bands were prestretched to approximately 50% of the initial length (initial length, 1.9 m), and then different bands were added when needed to reach a desirable intensity. For this purpose, different levels of elastic resistance (red, blue, black, silver, and gold elastic band colors) were allowed (Thera-Band CLX; The Hygenic Corp, Akron, OH, USA), alone or in combination. After each condition, participants were asked to rate the tolerability of that condition, according to the following scale: very well tolerated, tolerated, neutral, not well tolerated, and not tolerated. Finally, 24 and 48 hours after the session, participants were asked about possible adverse effects (bleeding, pain). In addition, they were asked to report any possible adverse event during the week after.

[H2] Data Analysis

EMG data processing was performed using custom-made algorithms implemented in MATLAB (version R2015a; The MathWorks, Inc, Natick, MA, USA) software. For the analysis, all raw EMG signals obtained during the exercises were digitally filtered with Butterworth fourth-order high-pass filtering at 10 Hz and a moving root-mean-square (RMS). The RMS routine was performed using a smoothing filter/window of 500 milliseconds (250 milliseconds backward and 250 milliseconds forward from each data point) across the entire signal (ie, across all contractions). For each individual muscle, the peak RMS EMG value of each of the 3 repetitions performed at each condition was determined, and the average value of these 3 repetitions (ie, averaged peak) was then normalized to the maximal RMS EMG value obtained during the MVIC collection.

Because of this procedure, the “peak” EMG level included 500 milliseconds and not just the single data point of the raw EMG value.

An a priori power analysis was conducted with G*Power (version 3.1.9.2; Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany) software to calculate the sample size. With the present study design, assuming a medium effect size ($f = 0.30$), an alpha value of .05, a power of 0.80, and a correlation among repeated measures of 0.50, the total sample size required is 11 participants.

A linear mixed model (Proc Mixed; SAS version 9.4; SAS Institute, Cary, NC, USA) was used to determine whether differences existed between conditions (elastic resistance, machine resistance, and no external resistance) for each respective muscle. The RMS normalized EMG (nEMG) value was the dependent variable. Participant was included in the statistical model as a random factor. Values are reported as least square means (95% CI) unless otherwise stated. *P* values of <.05 were considered statistically significant. In addition, the effect size (Cohen *d*) was calculated and described as follows: <0.2 = trivial effect; 0.2 to 0.5 = small effect; 0.5 to 0.8 = moderate effect; and >0.8 = large effect.

[H2] Role of the Funding Source

This study was supported by an investigator-initiated research grant (H15-29504) from Baxalta US Inc, Bannockburn, IL, USA, now part of Takeda

Pharmaceuticals. Takeda does not necessarily endorse, support, or agree with any or all of the content.

[H1] Results

Table 1 shows complete demographic and descriptive data for the participants. Five of the 11 participants received prophylaxis treatment 3 times per week, 5 received prophylaxis treatment twice per week, and 1 received daily prophylaxis treatment. Eight participants reported an ABR in the lower limbs of 0, 2 participants had an ABR of 1 (in the left knee and the right ankle), and 1 participant had an ABR of 2 (left and right ankles). Most of the participants (54%) performed leisure-time physical activity 2 or 3 times per week but had no resistance training experience. Table 2 shows the leisure-time physical activity and resistance training experience of the participants.

All participants were able to perform all conditions satisfactorily and were thus included in the following results. After receiving feedback from all participants, no adverse effects were reported 24 hours, 48 hours, or 1 week after the experimental session. In the knee extension exercise, rectus femoris RMS nEMG values during the elastic resistance and machine resistance conditions were similar; 29% to 30% higher activity ($P < .01$) and a large effect size were obtained during these conditions than during the non-external resistance condition. In the ankle plantar flexion exercise, the gastrocnemius lateralis RMS nEMG value was higher (34%; $P = .048$; moderate effect size) during the machine resistance condition than without external resistance, and the nEMG values during the elastic resistance and other 2 conditions were similar.

Complete RMS nEMG results are reported in Table 3. The Supplementary Figure (available at <https://academic.oup.com/ptj>) shows original representative EMG recordings from the rectus femoris muscle during the different conditions.

All of the exercises performed were tolerated by the participants with a general reported high tolerance. Table 4 shows complete tolerability data.

[H1] Discussion

The purpose of the present study was to quantify lower limb muscle activity and to evaluate safety (tolerability and adverse events) of 2 common therapeutic exercises (knee extension and ankle plantar flexion) performed in different conditions (elastic resistance, machine resistance, and no external resistance). The main findings of the study were the similar agonist muscle activity levels and high tolerability for the elastic resistance and machine resistance conditions, without adverse effects 24 hours, 48 hours, or 1 week after the experimental session.

Several studies reported similar levels of muscle activity in comparisons of elastic bands with free weights or machines in people who were healthy. Importantly, elastic bands provide in conjunction with length of lever arm a bell-shaped torque curve, in spite of the ascending resistance provided by this equipment.^{28–30}

For instance, Matheson et al³¹ found that in adults who were healthy, the elastic resistance knee extension and the free-weight variation yielded similar rectus femoris and vastus lateralis activity levels during both concentric and eccentric phases, also resulting in similar peak loads at the same angular velocity. In the same vein, other studies with adults who were healthy found comparable quadriceps muscle activity levels^{15,16} during the knee extension when the exercises were performed with machine resistance and elastic resistance. In contrast, different results have been reported in clinical populations.^{10,13} For example, in patients with chronic stroke, the machine-based knee extension exercise resulted in higher vastus medialis activity in the nonparetic leg and higher vastus lateralis activity in the paretic leg.¹⁰ However, similar activity was reported in the vastus lateralis muscle in the nonparetic leg, whereas no changes were found in the biceps femoris and semitendinosus muscles.¹⁰ Likewise, in the present population of people with hemophilia, we found similar biceps femoris activity levels and similar gastrocnemius lateralis activity levels during the different conditions. Interestingly, we found a higher tibialis anterior activity level during knee extension with elastic resistance than with the other conditions, in which there were no differences. This is likely due to the direct attachment of the elastic band to the feet (in dorsiflexion), generating more tension and activity in the tibialis anterior muscle during performance of the exercise. This increased intermuscular coordination may provide a more functional EMG pattern since hip flexor and dorsiflexor muscles are the main synergistic contributors during the swing gait phase.³²

In agreement with our hypothesis, we found comparable gastrocnemius lateralis activity levels during plantar flexion exercise with elastic resistance and machine resistance, although with a borderline significant result and a moderate effect size favoring the machine. These results may be explained by the higher activity levels of the rectus femoris and biceps femoris muscles during ankle plantar flexion with machine resistance than with the other conditions, which could have resulted in greater force production. It is plausible that isolating the movement with the ankle plantar flexor muscles and the hip is more difficult using the machine, as a closed kinetic chain exercise, in comparison with the other conditions, performed in an open kinetic chain way. It is also likely that a lack of stabilization of proximal joints contributed to the higher activity level in the thigh musculature during the machine variation. To our knowledge, there is no previous research in this field; therefore, future studies are needed to confirm differences between elastic resistance and machine resistance during the ankle plantar flexion exercise. Another finding favoring the machine variation was the absence of difference between the elastic resistance version and the non-external resistance condition. Altogether, the RMS nEMG percentage obtained and the fact that several elastic bands were used to achieve the intensity, elastic resistance may be less efficient and feasible to reach high intensities. In addition, machine-based ankle plantar flexion showed lower antagonist (ie, tibialis anterior muscle) coactivation than the other variations, indicating greater efficiency during this condition and lower joint compression; thus, machine-based ankle plantar flexion is a more desirable choice, especially in people with joint arthropathy. Even though some coactivation is necessary for joint stabilization, 1 study showed that augmented muscle coactivation accelerated loss of cartilage volume and thus the

progression of knee osteoarthritis.³³ The lower coactivation during the machine variation may be explained by a greater force output and/or greater stability than during the other conditions.

Importantly, all exercises and conditions were well tolerated and there were no associated adverse effects after a single bout of training. As expected, the non-external resistance conditions had the greatest tolerability rates. Interestingly, the elastic resistance conditions had slightly better tolerability than the machine resistance condition, indicating that elastic resistance during these exercises is more user-friendly for people with hemophilia. Previous data have also showed general high tolerability when using elastic resistance during different lower limb exercises performed during bed rest.³⁴ High patient satisfaction has been associated with higher levels of participation.³⁵ The reported tolerability rates provide the level of satisfaction with each different exercise and condition and together with the RMS nEMG values, provide valuable information that can help to prescribe proper exercise in people with hemophilia.

Previous studies suggested that exercises providing greater muscle activity would be more effective,^{26,36} although it remains difficult to establish whether EMG can be used to infer strength gains or hypertrophy.³⁷ It must also be considered that training intensity was based on “strong” levels of perceived exertion (6 on the Borg CR10 Scale), and that, based on previous studies showing a correlation between perceived exertion ratings, muscle EMG, and training loads, higher levels of muscle activity could

be expected with greater levels of perceived exertion. However, while high intensities maximize strength adaptations,^{38,39} low to moderate intensities can effectively improve muscular endurance^{38,39} and even induce strength gains among untrained participants, which could be the case of the present study. Importantly, a previous study found that biomechanically similar exercises with matched intensity resulted in comparable acute RMS nEMG values and also comparable muscle strength gains after a 5-week training period.⁴⁰ These data suggest that similar knee extensor strength could be expected with elastic resistance and machine resistance when both are performed under the same controlled conditions.

The major limitation of our study is the small sample size. However, the number of participants was sufficient in accordance with an a priori power analysis. The use of only 1 experimental session and the reliability of EMG recordings can be considered another limitation. However, procedures were standardized and exercises performed in a controlled manner, so values are likely reflecting the true intensities of muscle activity. In addition, it is plausible that using 2 MVIC contractions would have provided a more reliable maximum value. However, it seems that the MVICs were adequate, since most RMS nEMG values in the agonist muscles during the external resistance conditions were nearly 50%, which provides a similar moderate intensity, according to the Borg CR10 Scale intensity used. It should be acknowledged that although previous studies found a moderate to strong association among perceived exertion, actual loading, and nEMG values in participants who were healthy,^{26,27} it is an assumption that the same relationship exists in the current study cohort. However, although other

methods for assessing relative intensity (such as using a certain repetition maximum) have been investigated more thoroughly, the literature generally shows similar levels of agonist muscle activity when perceived exertion is matched^{26,27} and in people with hemophilia.⁴¹ An additional advantage of using perceived exertion to assess intensity is that is less time-consuming, stressing and fatiguing than typical maximal strength tests, which can be especially beneficial for people with hemophilia.

Assessing tolerability and adverse events solely after a single bout of exercise is a study limitation; progressive resistance exercise programs require multiple sessions, and both the frequency and duration of such programs to safely strengthen the muscles of the lower extremity remains to be determined. Finally, since adverse events were self-reported by the participants, subclinical bleeding or minor adverse events could have been overlooked. However, it seems that with an appropriate coverage factor, people can avoid major adverse events after performing these exercises at moderate intensity.

[H1] Conclusion

Elastic bands and machines are safe, feasible, and efficient for people who have severe hemophilia and are undergoing prophylactic treatment, providing comparable muscle activity levels during knee extension and ankle plantar flexion exercises performed at moderate intensity. However, when available, machine-based resistance exercise may be the preferred method of plantar flexor muscle training to help optimize activation

of the agonist muscle while minimizing joint stress due to lower coactivation of the antagonist muscle.

Because elastic bands are portable and are tolerated slightly better than machines, they can be considered a real alternative for supervised rehabilitation programs and the first choice for home-based training in people who have severe hemophilia and are receiving prophylactic treatment.

Author Contributions and Acknowledgments

Concept/idea/research design: J. Calatayud, S. Pérez-Alenda, L.L Andersen, J. Casaña

Writing: J. Calatayud

Data collection: J. Calatayud, A. Escriche-Escuder, J. Casaña

Data analysis: J. Calatayud, J.J. Carrasco, C. Cruz-Montecinos, L.L Andersen

Project management: S. Pérez-Alenda, F. Querol, J. Casaña

Fund procurement: S. Pérez-Alenda, F. Querol

Providing participants: S. Pérez-Alenda, S. Bonanad, F. Querol

Providing facilities/equipment: S. Pérez-Alenda, F. Querol, J. Casaña

Providing institutional liaisons: S. Pérez-Alenda, S. Bonanad, F. Querol, J. Casaña

The authors thank the participants for their contribution to the study.

Ethics Approval

The study conformed to the Declaration of Helsinki and was approved by the local ethics committee (ref. no. H1461147538087). All participants were informed about the purpose and content of the investigation. Written informed consent was obtained from all individual participants in the study.

Funding

This study was supported by an investigator-initiated research grant (H15–29504) from Baxalta US Inc, Bannockburn, IL, USA, now part of Takeda Pharmaceuticals.

Disclosures

The authors completed the ICJME Form for Disclosure of Potential Conflicts of Interest and reported no conflicts of interest. Data reported in this study are part of a research project investigating muscle activity during different exercises in people with hemophilia.

References

1. Rodriguez-Merchan EC. Musculoskeletal complications of hemophilia. *HSS J*. 2010;6:37-42.
2. Srivastava A, Brewer AK, Mauser-Bunschoten EP, et al. Guidelines for the management of hemophilia. *Haemophilia*. 2013;19:e1-e47.
3. Kurz E, Herbsleb M, Grassme R, Anders C, Hilberg T. Trunk muscle activation characteristics in patients with severe haemophilia. *Haemophilia*. 2017;23:122-128.
4. Stephensen D, Taylor S, Bladen M, Drechsler WI. Relationship between physical function and biomechanical gait patterns in boys with haemophilia. *Haemophilia*. 2016;22:e512-e518.
5. Stephensen D, Drechsler WI, Scott OM. Influence of ankle plantar flexor muscle architecture and strength on gait in boys with haemophilia in comparison to typically developing children. *Haemophilia*. 2014;20:413-420.
6. Lobet S, Lambert C, Hermans C. Stop only advising physical activity in adults with haemophilia... prescribe it now! The role of exercise therapy and nutrition in chronic musculoskeletal diseases. *Haemophilia*. 2016;22:e554-e556.
7. Patel HP, Syddall HE, Jameson K, et al. Prevalence of sarcopenia in community-dwelling older people in the UK using the European Working Group on Sarcopenia in Older People (EWGSOP) definition: findings from the Hertfordshire Cohort Study (HCS). *Age Ageing*. 2013;42:378-384.
8. Goto M, Takedani H, Nitta O, Kawama K. Joint function and arthropathy severity in patients with hemophilia. *J Jpn Phys Ther Assoc*. 2015;18:15-22.
9. Rondanelli M, Faliva M, Monteferrario F, et al. Novel insights on nutrient management of sarcopenia in elderly. *Biomed Res Int*. 2015;2015:524948.
10. Vinstrup J, Calatayud J, Jakobsen MD, et al. Electromyographic comparison of elastic resistance and machine exercises for high-intensity strength training in patients with chronic stroke. *Arch Phys Med Rehabil*. 2016;97:429-436.
11. Frost DM, Cronin J, Newton RU. A biomechanical evaluation of resistance: fundamental concepts for training and sports performance. *Sports Med*. 2010;40:303-326.
12. Mulvany R, Zucker-Levin AR, Jeng M, et al. Effects of a 6-week, individualized, supervised exercise program for people with bleeding disorders and hemophilic arthritis. *Phys Ther*. 2010;90:509-526.

13. Sundstrup E, Jakobsen MD, Andersen CH, et al. Evaluation of elastic bands for lower extremity resistance training in adults with and without musculo-skeletal pain. *Scand J Med Sci Sports*. 2014;24:e353-e359.
14. Jakobsen MD, Sundstrup E, Andersen CH, Persson R, Zebis MK, Andersen LL. Effectiveness of hamstring knee rehabilitation exercise performed in training machine vs. elastic resistance: electromyography evaluation study. *Am J Phys Med Rehabil*. 2014;93:320-327.
15. Aboodarda SJ, Shariff MAH, Muhamed AMC, Ibrahim F, Yusof A. Electromyographic activity and applied load during high intensity elastic resistance and nautilus machine exercises. *J Hum Kinet*. 2011;30:5-12.
16. Jakobsen MD, Sundstrup E, Andersen CH, et al. Muscle activity during knee-extension strengthening exercise performed with elastic tubing and isotonic resistance. *Int J Sports Phys Ther*. 2012;7:606-616.
17. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet*. 2007;370:1453-1457.
18. Pettersson H, Ahlberg A, Nilsson IM. A radiologic classification of hemophilic arthropathy. *Clin Orthop*. 1980:153-159.
19. Iorio A, Keepanasseril A, Foster G, et al. Development of a Web-Accessible Population Pharmacokinetic Service—Hemophilia (WAPPS-Hemo): study protocol. *JMIR Res Protoc*. 2016;5:e239.
20. Hilliard P, Funk S, Zourikian N, et al. Hemophilia Joint Health Score reliability study. *Haemophilia*. 2006;12:518-525.
21. Kurtze N, Rangul V, Hustvedt B-E, Flanders WD. Reliability and validity of self-reported physical activity in the Nord-Trøndelag health study: HUNT 1. *Scand J Public Health*. 2008;36:52-61.
22. Hermens HJ, Freriks B, Disselhorst-Klug C, Rau G. Development of recommendations for SEMG sensors and sensor placement procedures. *J Electromyogr Kinesiol*. 2000;10:361-374.
23. Kendall FP, McCreary EK, Provance PG, Rodgers MM, Romani WA. *Muscles: Testing and Function With Posture and Pain*. 5th ed. Baltimore, MD: Lippincott Williams & Wilkins; 2005.
24. Buckley JP, Borg GAV. Borg's scales in strength training; from theory to practice in young and older adults. *Appl Physiol Nutr Metab*. 2011;36:682-692.
25. Garber CE, Blissmer B, Deschenes MR, et al. American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy

- adults: guidance for prescribing exercise. *Med Sci Sports Exerc.* 2011;43:1334-1359.
26. Andersen LL, Andersen CH, Mortensen OS, Poulsen OM, Bjørnlund IBT, Zebis MK. Muscle activation and perceived loading during rehabilitation exercises: comparison of dumbbells and elastic resistance. *Phys Ther.* 2010;90:538-549.
 27. Brandt M, Jakobsen MD, Thorborg K, Sundstrup E, Jay K, Andersen LL. Perceived loading and muscle activity during hip strengthening exercises: comparison of elastic resistance and machine exercises. *Int J Sports Phys Ther.* 2013;8:811-819.
 28. Aboodarda SJ, Hamid MSA, Muhamed AMC, Ibrahim F, Thompson M. Resultant muscle torque and electromyographic activity during high intensity elastic resistance and free weight exercises. *Eur J Sport Sci.* 2013;13:155-163.
 29. Simoneau GG, Bereda SM, Sobush DC, Starsky AJ. Biomechanics of elastic resistance in therapeutic exercise programs. *J Orthop Sports Phys Ther.* 2001;31:16-24.
 30. Hughes CJ, Hurd K, Jones A, Sprigle S. Resistance properties of Thera-Band tubing during shoulder abduction exercise. *J Orthop Sports Phys Ther.* 1999;29:413-420.
 31. Matheson JW, Kernozek TW, Fater DC, Davies GJ. Electromyographic activity and applied load during seated quadriceps exercises. *Med Sci Sports Exerc.* 2001;33:1713-1725.
 32. Cruz-Montecinos C, Pérez-Alenda S, Cerda M, Maas H. Neuromuscular control during gait in people with haemophilic arthropathy. *Haemophilia.* 2019;25:e69-e77.
 33. Hodges PW, van den Hoorn W, Wrigley TV, et al. Increased duration of co-contraction of medial knee muscles is associated with greater progression of knee osteoarthritis. *Man Ther.* 2016;21:151-158.
 34. Vinstrup J, Skals S, Calatayud J, et al. Electromyographic evaluation of high-intensity elastic resistance exercises for lower extremity muscles during bed rest. *Eur J Appl Physiol.* 2017;117:1329-1338.
 35. Weingarten SR, Stone E, Green A, et al. A study of patient satisfaction and adherence to preventive care practice guidelines. *Am J Med.* 1995;99:590-596.
 36. Andersen LL, Magnusson SP, Nielsen M, Haleem J, Poulsen K, Aagaard P. Neuromuscular activation in conventional therapeutic exercises and heavy resistance exercises: implications for rehabilitation. *Phys Ther.* 2006;86:683-697.
 37. Vigotsky AD, Halperin I, Lehman GJ, Trajano GS, Vieira TM. Interpreting signal amplitudes in surface electromyography studies in sport and rehabilitation sciences. *Front Physiol.* 2017;8:985.

38. Jenkins NDM, Miramonti AA, Hill EC, et al. Greater neural adaptations following high- vs. low-load resistance training. *Front Physiol.* 2017;8:331.
39. Schoenfeld BJ, Peterson MD, Ogborn D, Contreras B, Sonmez GT. Effects of low- vs. high-load resistance training on muscle strength and hypertrophy in well-trained men. *J Strength Cond Res.* 2015;29:2954-2963.
40. Calatayud J, Borreani S, Colado JC, Martin F, Tella V, Andersen LL. Bench press and push-up at comparable levels of muscle activity results in similar strength gains. *J Strength Cond Res.* 2015;29:246-253.
41. Calatayud J, Pérez-Alenda S, Carrasco JJ, et al. Upper-body exercises with external resistance are well tolerated and enhance muscle activity in people with hemophilia. *Phys Ther.* 2019;99:411-419.

Table 1.Demographic and Descriptive Data^a

Characteristic	Mean	SD	Minimum	Maximum
Age (y)	34.7	9.1	21.0	47.0
Height (cm)	172.5	9.0	157.0	187.0
Body mass (kg)	75.7	18.0	51.1	116.6
HJHS for dominant knee	2.0	4.4	0.0	11.0
HJHS for nondominant knee	2.5	4.7	0.0	14.0
HJHS for dominant ankle	4.7	3.1	0.0	9.0
HJHS for nondominant ankle	5.4	3.5	1.0	11.0
Pettersson score for dominant knee	1.8	4.1	0.0	13.0
Pettersson score for nondominant knee	1.6	3.7	0.0	12.0
Pettersson score for dominant ankle	4.8	5.7	0.0	13.0
Pettersson score for nondominant ankle	6.0	6.0	0.0	13.0
FVIII dose (IU/kg) (n = 10)	30.5	13.3	12.9	58.7
FIX dose (IU/kg) (n = 1)	56.0			
FVIII peak (IU/dL) (n = 10)	64.5	26.2	37.8	120.5
FIX peak (IU/dL) (n = 1)	44.3			
FVIII t _{1/2} (h) (n = 10)	13.0	4.5	7.0	18.8
FIX t _{1/2} (h) (n = 1)	28.5			

^aFIX = factor IX; FVIII = factor VIII; HJHS = Hemophilia Joint Health Score; t_{1/2} = half-life.

Table 2

Leisure-Time Physical Activity

Activity	No. (%) of Participants
Leisure-time physical activity	
Frequency	
Never	1 (9.09)
<1 time/wk	1 (9.09)
1 time/wk	1 (9.09)
2 or 3 times/wk	6 (54.55)
Almost daily	2 (18.18)
Intensity	
Take it easy	6 (60.00)
Push some	4 (40.00)
Nearly to exhaustion	
Duration	
<15 min	
16–30 min	1 (10.00)
30–60 min	4 (40.00)
>1 h	5 (50.00)
Resistance training	
Yes	2 (18.18)
No	9 (81.82)
Frequency	
2 times/wk	1 (50.00)
3 times/wk	1 (50.00)
Years of experience	
10	1 (50.00)
2	1 (50.00)
Intensity	
Moderate (60%–70%)	2 (100)

Table 3Root-Mean-Square (RMS) Normalized Electromyography (nEMG) Results^a

Measure	Mean (95% CI) RMS nEMG ^b With:			No External Resistance vs Elastic Resistance		No External Resistance vs Machine Resistance		Elastic Resistance vs Machine Resistance	
	No External Resistance	Elastic Resistance	Machine Resistance	<i>P</i>	Cohen <i>d</i>	<i>P</i>	Cohen <i>d</i>	<i>P</i>	Cohen <i>d</i>
Knee extension									
Rectus femoris	21 (8–34)	50 (38–63)	51 (39–64)	.002	1.481	.002	1.482	.91	0.084
Biceps femoris	7 (1–13)	14 (8–21)	15 (8–21)	.11	1.012	.10	0.533	.99	0.008
Gastrocnemius lateralis	5 (1–9)	10 (6–14)	7 (3–11)	.06	1.301	.45	0.733	.23	0.612
Tibialis anterior	5 (1–12)	23 (16–30)	10 (3–16)	<.001	1.200	.37	0.622	.008	1.036
Ankle plantar flexion									
Rectus femoris	2 (0–4)	3 (1–5)	6 (4–8)	.70	0.350	.019	0.687	.046	0.578
Biceps femoris	4 (1–9)	5 (0–10)	18 (12–23)	.83	0.132	<.001	0.995	.001	0.824
Gastrocnemius lateralis	42 (18–65)	44 (20–68)	76 (52–99)	.87	0.176	.048	0.677	.07	0.614
Tibialis anterior	50 (38–62)	42 (30–55)	15 (3–28)	.37	0.294	<.001	1.121	.003	1.54

^aElastic resistance = elastic band–based resistance; machine resistance = machine-based resistance.^bData are reported as % of RMS nEMG.

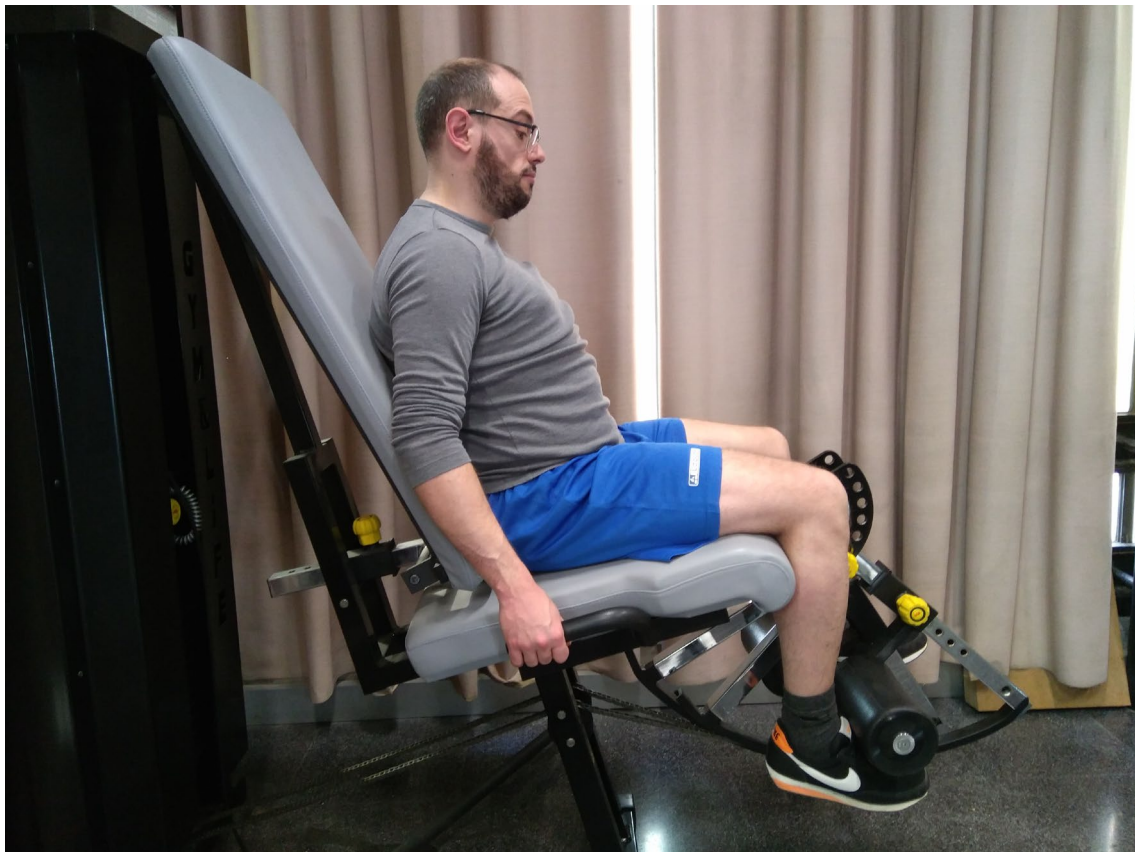
Table 4.Exercise Tolerability^a

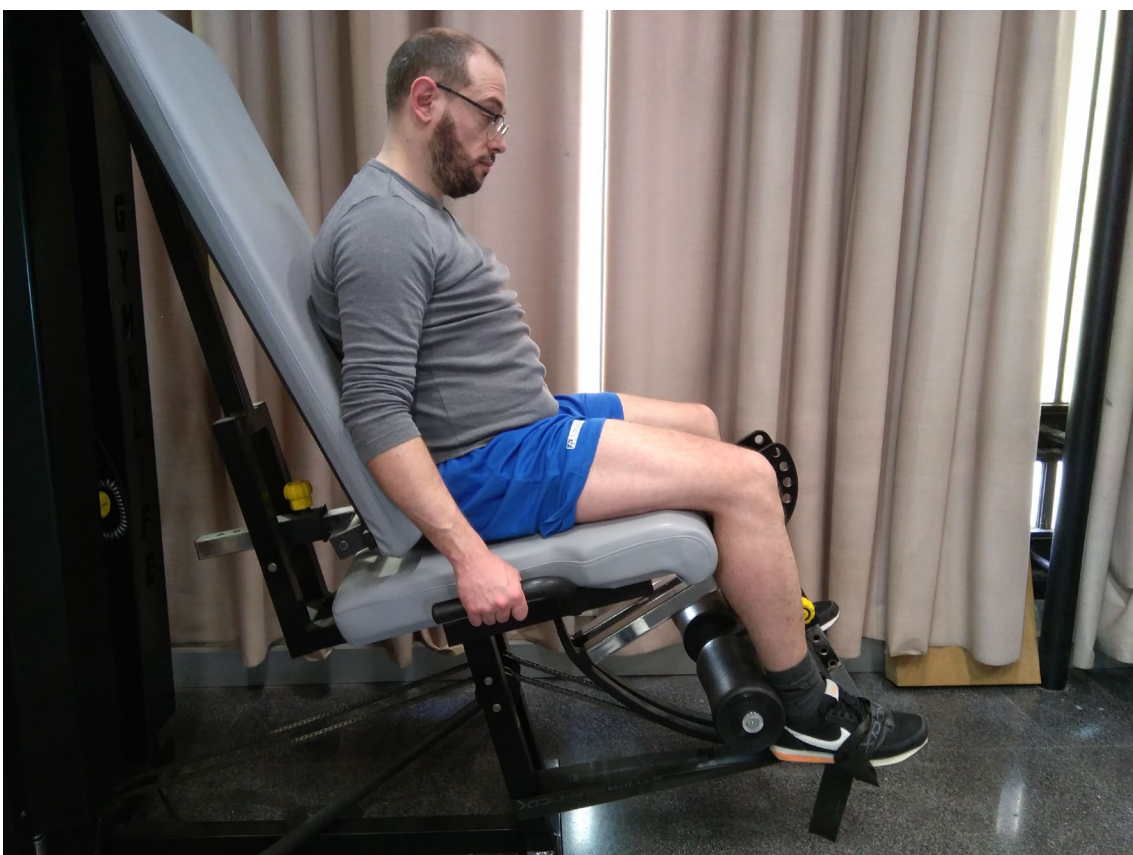
Tolerability	Knee Extension			Plantar Flexion		
	No External Resistance	Machine Resistance	Elastic Resistance	No External Resistance	Machine Resistance	Elastic Resistance
Very well tolerated	90.91	27.27	45.45	81.82	27.27	45.45
Tolerated	9.09	54.55	36.36	18.18	54.55	54.55
Neutral	0.00	9.09	18.18	0.00	9.09	0.00
Not well tolerated	0.00	9.09	0.00	0.00	9.09	0.00
Not tolerated	0.00	0.00	0.00	0.00	0.00	0.00

^aData are reported as percentages of participants. Elastic resistance = elastic band–based resistance; machine resistance = machine-based resistance.

Figure 1.

Illustrative example of the knee extension exercise with external band-based and machine-based resistance. (A) and (B) show the initial and final phases, respectively, of knee extension with the machine; (C) and (D) show the initial and final phases, respectively, of knee extension with elastic resistance.





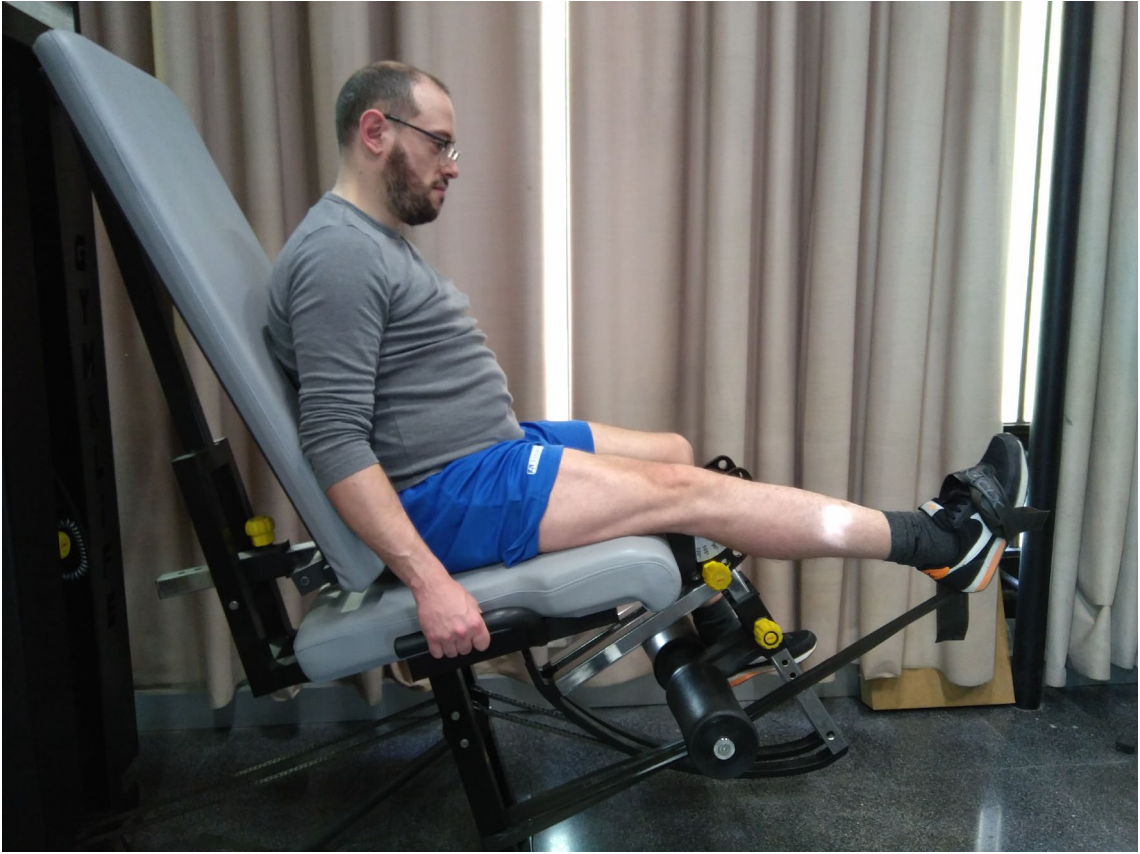


Figure 2.

Illustrative example of the ankle plantar flexion exercise with external band-based and machine-based resistance. (A) and (B) show the initial and final phases, respectively, of ankle plantar flexion with the machine; (C) and (D) show the initial and final phases, respectively, of ankle plantar flexion with elastic resistance.



