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ORIGINAL ARTICLE

Feasibility, safety and muscle activity during flywheel vs traditional strength training in adult patients with severe haemophilia

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Abstract

Introduction: Eccentric training has been associated with several specific physiological adaptations. The flywheel machine is one of the easiest ways of performing eccentric overload training. However, no studies evaluated its feasibility, safety and muscle activity in patients with haemophilia (PWH).

Aim: To evaluate feasibility and safety and compare muscle activity during flywheel vs weight machine knee extension exercise in severe PWH.

Methods: Eleven severe PWH [mean age of 33.5 (8.1) years] participated in this cross-sectional study after receiving prophylactic treatment. Surface electromyography (EMG) signals were recorded for the rectus femoris during the knee extension exercise performed with 2 different conditions (flywheel and weight machine) with matched intensity (6 on the Borg CR10 scale). Kinesiophobia was assessed before and after the experimental session. Participants were asked to rate tolerability of each condition. Adverse effects were evaluated 24 and 48 hours after the session.

Results: Kinesophobia did not increase after the experimental session, and no adverse effects were reported. At 60%-70% of the contraction cycle, the flywheel exercise showed higher (P = .024) eccentric rectus femoris muscle activity than the weight machine. In contrast, during the last 90%-100% of the contraction cycle, the traditional weight machine showed higher (P = .004) rectus femoris activity than the flywheel.

Conclusion: The knee extension exercise performed with the flywheel at moderate intensity is safe and well tolerated among severe PWH under adequate factor coverage. Importantly, the flywheel variation provides higher eccentric rectus femoris activity at the breaking force moment, while it provides lower eccentric muscle activity at the end of the cycle.

KEYWORDS
eccentric, flywheel, knee, strength, tolerability

1 | INTRODUCTION

Haemophilia is an inherited bleeding disorder caused by an X-linked deficiency of the clotting factor protein VIII (haemophilia A) or IX (haemophilia B).[1] Patients with severe haemophilia experience spontaneous bleedings into muscles and especially joints.[1] In fact, 90% of these patients will suffer joint disease,[2] with the knee as one of the most affected joints,[1] limiting activities of daily living and quality of life.

Strength training plays an important role in preventing and rehabilitating musculoskeletal problems in patients with haemophilia (PWH).[3] Among the different types of strength training, eccentric training has been widely investigated during the last years in healthy subjects, due to its unique characteristics. For instance, isolated eccentric contractions compared with isolated concentric contractions have greater neural[4] and metabolic efficiency at similar mechanical workloads.[5] In consequence, eccentric actions result in lower acute fatigue than concentric muscle actions.[6] Furthermore, eccentric actions have showed greater cortical activity,[7] increased muscle satellite cell proliferation 24 hours postexercise,[8] faster postexercise rise of protein synthesis,[9] higher recruitment of type II muscle fibres[10] and greater cross-education[11] than concentric actions. However, isolated eccentric training is difficult to apply and is not related to many daily life activities that require both concentric and eccentric contractions.[12] In this sense, one of the easiest ways of performing both types of contractions while having brief episodes of eccentric overload is using a flywheel machine. This technology employs isoinertial resistance, which allows for maximal concentric and eccentric actions.[13,14] On the contrary, in a traditional gravity-dependent machine (weight machine), the load lifted during the concentric phase limits the ability of optimally loading the eccentric phase of the movement (given its higher force capacity).

In spite of this, few investigations were conducted to evaluate the electromyographic response during this type of training in comparison with weight machines. These studies conducted with healthy samples found greater lower limb eccentric muscle activity during the flywheel than the traditional counterpart in a seated knee extension[14] and a squat.[15] Thus, whether eccentric overload training can be performed in PWH remains uninvestigated, likely due to the greater myofibre damage associated with this type of contractions when compared to concentric actions.[16] So far, this may have considered especially negative in PWH, where high stress derived from exercise has been typically avoided due to fear of producing bleedings and pain.

Due to the potential benefits showed in healthy subjects, this type of training could be also considered in preventive and rehabilitative musculoskeletal programmes for PWH. For instance, flywheel training could be especially used to properly load the eccentric phase of the movement, which could have some positive effects on preventing bleedings when being exposed to heavy eccentric forces or (eg decelerations) in daily life activities or other sports practice. However, a cautious approach is needed when implementing eccentric overload training in PWH for the first time as these patients may have increased fear of movement due to repeated bleeding episodes or injuries, especially when they are not familiarized with certain exercise and movements.

With this in mind, the purpose of this study was to evaluate feasibility and safety and compare muscle activity during flywheel vs weight machine knee extension exercise in severe PWH. We hypothesized that flywheel exercise would be feasible and safe, resulting in greater eccentric muscle activity than the weight machine.

2 | METHODS

2.1 | Participants

During June to July 2017 at a local hospital (University and Polytechnic Hospital La Fe, Valencia, Spain), patients at least 18 years old and diagnosed with severe haemophilia in prophylactic treatment were considered candidates for the present study. Exclusion criteria were (a) joint replacement in the previous year, (b) joint or muscle bleeding in the last 3 months, (c) presenting inhibitors to factor VIII or factor IX, or (d) any medical condition where exercise is contraindicated. A total of 11 severe PWH receiving prophylactic treatment (10 type A; 1 type B) voluntarily participated in the study, which was performed at the University of Valencia during July 2017. All participants were informed about the purpose and content of the investigation. Written informed consent was obtained from all participants of the study. The study conformed to the Declaration of Helsinki and was approved by the Local Ethical Committee (H1461147538087). Data reported in the present study are part of a research project investigating muscle activity during different exercises in PWH. This reporting of the article adheres to the STROBE guidelines.[17]

2.2 | Procedures

The following clinical variables were collected from the medical record: type of haemophilia, prophylaxis regimen, pharmacokinetic values (half-life ($t_{1/2}$) and peak level), Annual Bleeding Joint Rate (ABJR) and haemophilic arthropathy in lower limbs measured radiologically with the Pettersson score.[18]

Each patient took part in one 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. Two days before the experimental session, the participants received a video with the exercise that had to be performed in order to visualize the proper technique. The patients performed the experimental session 1-2 hours after receiving the prophylactic treatment.

During the experimental session, height (IP0955, Invicta Plastics Limited) and body mass (Tanita model BF- 350) were obtained. The degree of haemophilic arthropathy was clinically evaluated by using the Hemophilia Joint Health Score 2.1 (HJHS),[19] and subsequently, the Tampa Scale for Kinesiophobia (TSK-11)[20] was used to assess beliefs about fear of movement (higher scores denote higher kinesiophobia) and evaluate possible changes after performing the session with eccentric overload. Later, leisure-time physical activity and resistance training experience were assessed. Afterwards, the surface electromyographic (EMG) protocol started with the preparation of patients' skin. Electrodes were placed according to SENIAM recommendations[21] on the rectus femoris on the dominant side of the body. Pregelled bipolar silver/silver chloride surface electrodes (Blue Sensor N-00-S, Ambu A/S) were placed with an inter-electrode distance of 2 cm. The reference electrode was placed between the active electrodes, approximately 10 cm away from the muscle. All signals were acquired at a sampling frequency of 1 kHz, amplified and converted from analog to digital. To acquire the surface EMG signals produced during exercise, an ME6000P8 (Mega Electronics, Ltd.) biosignal conditioner was used. Prior to the exercise performance described below, a 5-second maximum voluntary isometric contraction (MVIC) was performed. First, participants performed a non-maximal practice trial to ensure that they understood the task. After this, they were asked to exert progressive contraction during 2 seconds and to maintain 3 seconds of maximal contraction without reaching a pain intensity greater than 4 of 10.

Before starting with the exercise performance, participants performed 2 sets of 3 low-intensity unilateral knee extensions to warm-up, with 1-min rest on both the weight machine (F&H Fitness Equipments) and the flywheel (EPTE® Inertial Concept). After this, EMG measurements started. Participants performed 3 knee extension repetitions with the 2 aforementioned different conditions in a random order and with a 2-minute rest interval. Both conditions were performed in a seated position with back support, with knee flexion angle of 90° and hip angle of 110°. Using the Borg CR10 scale,[22] participants were asked to apply an effort corresponding to 6 so exercise was matched across conditions.

During the flywheel exercise, a 2.8 kg*m^2 moment inertia was used. The patients were asked to exert force during the entire range of motion in the concentric phase of the movement and then resisting the inertial force during the first third of the eccentric phase, applying maximal effort to stop the movement at about 60-70° of knee flexion and subsequently start again the concentric phase[13] from the starting point. This demonstrated an eccentric overload during the last two-thirds of the eccentric phase.[13]

Participants were asked to rate how tolerated was each condition, according to the following 5-point scale: very tolerated, tolerated, neutral, not so much tolerated and not tolerated. After finishing the last condition, kinesiophobia was re-assessed. Finally, 24 and 48 hours after the session, all participants were asked about possible adverse effects (eg bleedings, pain).

2.3 | Data analysis

EMG data processing was performed using custom-made algorithms implemented in MATLAB (The MathWorks, Inc, version R2018b) software. During later analysis, all raw EMG signals obtained during the exercises were digitally filtered, consisting of (a) high-pass filtering at 10 Hz and (b) a moving root mean square (RMS). The RMS routine was performed using a smoothing filter/window of 500 ms (250 ms backwards and 250 ms forward from each data point) across the entire signal (ie across all contractions). Subsequently, the EMG signals were manually segmented to obtain each contraction. Finally, segmented signals were resampled to 1000 samples and normalized to the maximal RMS EMG obtained during the MVIC collection.

2.4 | Statistical analysis

To compare muscle activity between the two exercises, a time-series statistical analysis was applied by using the MATLAB-based spm1d-package for n-dimensional statistical parametric mapping.[23] The exercise comparisons were then carried out by using two-tailed independent-samples *t* test.

Pre-post differences in kinesiophobia data were evaluated using paired-sample *t* test or Wilcoxon signed-rank test depending on normality. Cohen's *d* effect was calculated when statistically significant differences were observed, and it was interpreted as small ≥0.2, medium ≥0.5 and large ≥0.8.

A *P*-value of <.05 was considered as statistically significant. MATLAB statistical library was used for the analyses.

An a priori power analysis was conducted in G*Power (3.1.9.2 version) software to calculate the sample size. With the present study design, assuming a medium effect size ($d = 0.50$), alpha = 0.05, power = 0.80, the total sample size required is 11 participants to obtain 33 signals per condition.

3 | RESULTS

Table 1 shows complete demographic and descriptive data. Table 2 shows complete leisure-time physical activity and resistance training experience data and table 3 results of tolerability.

After receiving feedback from all participants, no adverse effects were reported after the experimental session. Kinesiophobia data (Table 4) showed an absence of differences ($P = 1$) between pre- and postsession scores, except for the item 3 ($P = .03$, $d = 0.93$) ('My body is telling me I have something dangerously wrong') in which the median has increased by one point.

At 60%-70% of the contraction cycle, the flywheel exercise showed higher ($P = .024$, $d = 0.61$) eccentric rectus femoris activity (mean (SD) [confidence interval at 95%] = 36.6 (20.9) [31.8:41.4] % of MVIC) than the weight machine (26.9 (8.6) [22.1:31.7] % of MVIC) (Figure 1). In contrast, during the last 90%-100% of the contraction cycle, the weight machine showed higher ($P = .004$, $d = 0.73$) rectus femoris activity (14.1 (6.1) [12.7:15.5] % of MVIC) than the flywheel exercise (10.5 (5.5) [9.1:11.9] % of MVIC).

4 | DISCUSSION

The main and novel findings of the present study are that flywheel exercise training at moderate intensities is feasible and safe and

TABLE 1 Demographic and descriptive data

	Mean	SD	Min	Max
Age (y)	33.5	8.1	21.0	47.0
Height (cm)	174.0	9.3	157.0	187.0
Body mass (kg)	82.6	29.4	51.1	152.7
Hemophilia Joint Health Score dominant knee	1.0	3.3	0.0	11.0
Hemophilia Joint Health Score non-dominant knee	2.0	4.7	0.0	14.0
Hemophilia Joint Health total score	23.2	14.1	5.0	54.0
Pettersson dominant knee	0.7	1.8	0.0	6.0
Pettersson non-dominant knee	1.6	3.7	0.0	12.0
Factor VIII dose (International Units/kg) (n = 10)	31.2	12.5	16.7	58.7
Factor IX dose (International Units/kg) (n = 1)	56.0	—	—	—
Factor VIII peak (n = 10)	67.3	24.5	44.4	120.5
Factor IX peak (n = 1)	44.3	—	—	—
Factor VIII $t_{1/2}$ (h) (n = 10)	12.1	4.4	7.0	18.8
Factor IX $t_{1/2}$ (h) (n = 1)	28.5	—	—	—
Prophylaxis frequency	2 times/wk		3 times/wk	
	5 (45.5%)		6 (54.5%)	
Annual Bleeding Joint Rate in lower limbs	0	1		2
	8 (72.7%)	2 (18.2%)		1 (9.1%)

TABLE 2 Leisure-time physical activity

Frequency	N (%)
Never	2 (18.18)
<1 time/wk	1 (9.09)
1 time/wk	1 (9.09)
2-3 times/wk	5 (45.45)
Almost daily	2 (18.18)
Intensity	
Low	5 (55.55)
Moderate	4 (44.44)
High	—
Duration	
<15 min	—
16-30 min	1 (11.11)
30-60 min	4 (44.44)
>1 h	4 (44.44)
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 y	1 (50.00)
2 y	1 (50.00)
Intensity	
Moderate (60%-70%)	2 (100)

TABLE 3 Exercise tolerability

	Flywheel machine	Weight machine
Very tolerable	45.5	36.4
Tolerable	36.4	45.5
Neutral	9.1	9.1
Little tolerable	9.1	9.1
Not tolerable	0.0	0.0

Note: Data are reported as percentages of participants.

provides higher and lower rectus femoris activity at 60%-70% and at the end of the contraction cycle, respectively. This is the first study testing feasibility, safety and muscle activity during an eccentric overload exercise in severe PWH. The present results may help to expand preventive and rehabilitative options and improving daily life or sports activities, especially those with sudden decelerations or marked eccentric forces such as descending stairs or walking on a ramp.

While no difference was noted at the first half of the cycle, the flywheel machine provided greater eccentric muscle activity at 60%-70% of the cycle (breaking force moment), with a moderate effect size. Previous studies found greater peak forces (15%-30%) during the eccentric phase than at the preceding concentric action when the subject resists the force, creating an eccentric overload.[13] Only a study[14] compared EMG data between the knee extension with a weight machine and a flywheel, albeit in contrast with our study, the latter condition was performed with maximal intensity and in healthy patients. In line with our results, authors reported that the flywheel

TABLE 4 Kinesiophobia results

Item number	TSK-11 Pre					TSK-11 Post					P-value
	Median	Q1	Q3	Mean	SD	Median	Q1	Q3	Mean	SD	
1	2.0	1.3	3.0	2.3	1.1	2.0	1.0	2.8	2.1	1.1	.63
2	3.0	2.0	4.0	2.8	1.7	3.0	2.0	3.0	2.5	0.9	.53
3	2.0	1.3	2.0	1.9	0.7	3.0	2.0	3.8	2.7	1.0	**.03**
4	3.0	1.0	3.8	2.5	1.3	3.0	2.0	4.0	2.7	1.2	.75
5	2.0	1.0	3.5	2.2	1.3	2.0	2.0	2.8	2.7	1.0	1.00
6	3.0	2.0	3.8	2.7	1.0	3.0	1.0	3.8	2.5	1.3	.81
7	3.0	2.0	3.0	2.6	0.9	2.0	2.0	2.8	2.4	0.9	.53
8	3.0	2.3	4.0	3.1	1.0	3.0	2.0	3.8	2.9	0.8	.75
9	1.0	1.0	1.8	1.5	0.9	1.0	1.0	1.8	1.4	0.67	1.00
10	2.0	2.0	4.0	2.7	1.0	2.0	2.0	3.8	2.7	0.9	1.00
11	2.0	1.3	4.0	2.5	1.3	2.0	1.3	4.0	2.5	1.3	.91
Total	28.0	22.3	32.3	26.7	6.1	25.0	21.3	33.0	26.7	7.8	1.0

Significant differences are shown in bold.

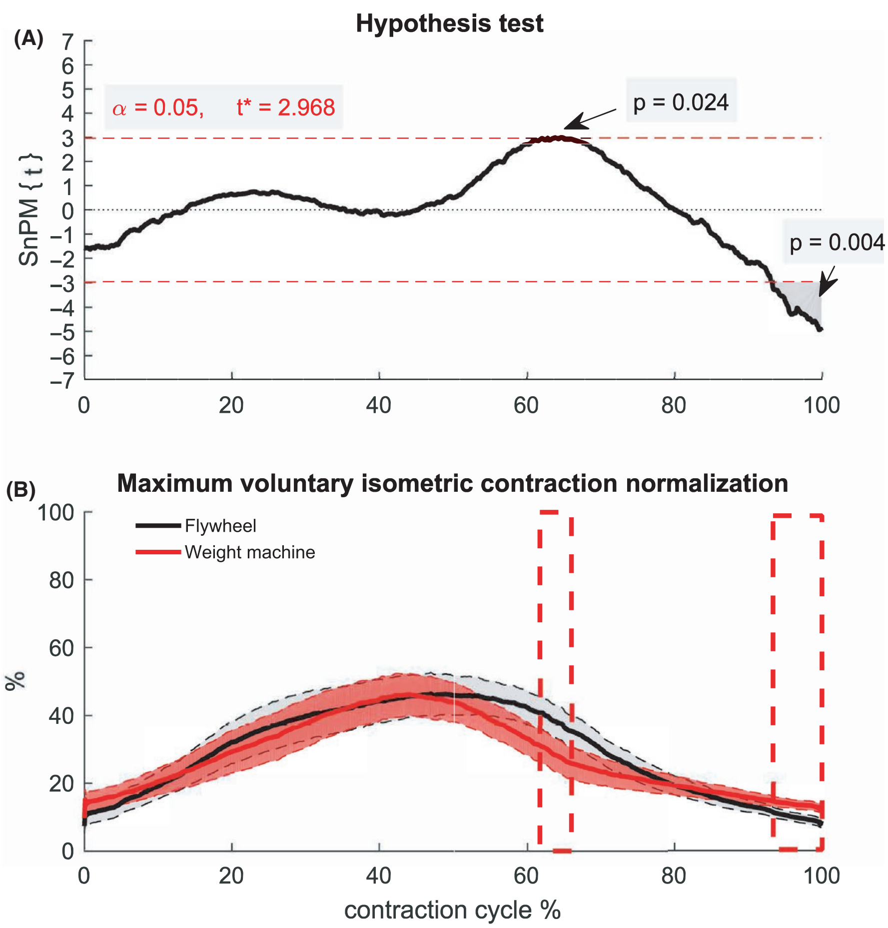

FIGURE 1 A, Hypothesis *t* test (t) comparison between both conditions using statistical parametric mapping (SPM) analysis. The horizontal red dashed line indicates $P < .05$ level. Grey zones indicate regions with statistically significant differences. B, Surface electromyography comparison between flywheel (red) and weight machine (black). Data are expressed as mean and 95% confidence intervals

variation provided greater activity at the eccentric phase than the weight machine.[14] However, at this study, differences between both variations at the eccentric phase were more evident at the last third of the contraction, especially at 90°, while in our study we found this at the first third of the eccentric phase, according to our instruction to resist the inertial force at that moment. In consequence, at the end of the eccentric phase during the flywheel condition we found the lowest activity of the whole contraction cycle—together with the one at the beginning of the concentric phase. In fact, we found that the weight machine provided greater EMG than the flywheel in this point, likely due to the very low inertial load after having applied maximal effort to stop the movement before starting with the subsequent concentric phase. In addition, according to previous studies,[14,24] we found the highest quadriceps muscle activity during the weight machine at near full extension in the concentric phase.

A recent study[24] found that mean quadriceps eccentric EMG was greater at the flywheel leg press than at the knee extension with a weight machine, while no difference was found during the concentric phase. However, it must be considered that the study used different exercises, and indeed, authors found a greater relative participation of the rectus femoris muscle at the knee extension than at the leg press.[24] As could be expected due to the greater neural efficiency,[4] and according to the previous study,[24] we found that the eccentric phase of the knee extension showed lower EMG signal than the concentric phase.

We believe that the absence of EMG differences during the concentric phase—matched by using the rate of perceived exertion—denotes that the Borg CR10 scale could be helpful to prescribe intensity during flywheel exercise. This is in line with other studies[25,26] reporting comparable muscle activity in upper or lower body exercises when the same exercise is performed with different equipment and the intensity is matched with the Borg CR10 scale. Future studies should validate this approach to prescribe flywheel exercise intensity, which has been typically performed at maximal effort (ie maximal intensity).

When performed at maximal effort, flywheel exercise is effective in increasing muscle strength and muscle size among healthy subjects.[12] Even so, it is plausible that the moderate intensity used in our study could provide positive adaptations in PWH, especially where the highest eccentric peak was found. In fact, light-moderate intensities can enhance muscular endurance even in well-trained subjects[27] and increase maximal strength in untrained subjects.[28] Thus—and considering the absence of adverse events—the flywheel could be considered as an alternative to traditional weight machine, providing a different stimulus and adding variety to training. It is worth mentioning that, in spite of the lower EMG signal found at the end of the eccentric phase with the flywheel, it is unlikely that such a low intensity (below 20% MVIC) would result in a positive adaptation. However, future experimental studies are needed to confirm these hypotheses and to explore the use of higher intensities during flywheel training among PWH with a close prophylactic control. Importantly, the type of exercise and intensities used in the present study appeared to be safe since patients did not report adverse events. Patients reported that there were no adverse effects (bleedings, pain) after the session. This finding is of major relevance, as bleedings from participation in physical exercise are a big concern not only among these patients but also for their physicians. In spite of the greater muscle damage associated with eccentric contractions when compared to concentric actions,[16] we did not use maximal effort and patients only performed 3 repetitions at each intensity. The warm-up performed in our study may have minimized muscle damage after the eccentric overload exercise.[29] In fact, in patients without resistance training experience—as in the present study—whom are more prone to suffer muscle damage,[30] performing proper warm-up could be even more relevant. A previous study[31] found that a long length of rectus femoris during eccentric exercise caused lower muscle damage than short length contractions. In our study, patients were asked to break the movement at 60-70° of knee flexion, which may have contributed to the safety.

Regarding kinesiophobia, we only found a one-point increase at the item 3. However, this item is not directly related to physical activity, and importantly, the global score was unchanged. In addition, it is unlikely that a single one-point increase will result in a clinically relevant change, although future studies are needed to corroborate whether the TSK-11 is sensitive and specific enough to detect changes after a single training session. It is plausible that due to the absence of high kinesiophobia levels in our sample, it was more difficult to find a difference, especially after only a session. An increased kinesiophobia normally causes refraining from exercise to avoid painful actions, which finally results in worsened physical condition, with greater disability and probability of depression.[32] Refraining from exercise can be especially negative for PWH, since muscle weakness and atrophy can increase pain and bleeding risk.[33]

Exercise tolerability was in general 'very tolerable' and 'tolerable'. Importantly, none of the patients experienced the exercise as 'non-tolerable' suggesting that even higher intensities could have been tolerated in many of the patients. It is important to distinguish between tolerability and occurrence of adverse events, since patients can feel that a certain exercise is not tolerable due to discomfort or fear of movement, but this does not necessarily result in adverse events. Nevertheless, perceived tolerability may be an important tool in the individual planning of exercise intensity among these patients. In addition, tolerability may be linked with patient's satisfaction, which is a relevant factor for treatment adherence.[34]

Another barrier to adherence in people with chronic pain conditions can be pain exacerbation with exercise.[35] It is known that the motor performance can be bi-directionally modulated by expectations, placebo and nocebo effects.[36] However, how expectations (positive or negative) and pain intensity interact with the nocebo and exercise intensity in PWH remains unknown and future studies are needed, particularly in those patients with high levels of pain. Recent evidence from a systematic review with meta-analyses concluded that pain during therapeutic exercise for chronic musculoskeletal pain need not be a barrier to successful outcomes.[37] In fact, this study[37] found that protocols using exercises into pain had a small but significant benefit over pain-free exercises in the short term (likely due to the higher exercise dosage). Another example where exercise with pain is usually performed is among patients with Achilles tendinopathy, where a level up to 5/10 at the numerical pain rating scale has been considered acceptable.[38] Importantly, pain does not correlate with tissue damage.[39] The criteria for performing a contraction up to a pain level of 4/10 were selected based on previous studies in PWH,[25,26] where a single strength training session with moderate intensity was well tolerated and did not cause adverse events.

The main limitation of the study is the small sample size, although sufficient according to an a priori power analysis. In addition, safety was only based on self-reported information without clinical or ultrasound assessment. Moreover, we only performed two exercises and thus safety needs to be further confirmed after a whole training session. However, as in research with, eg, medicine, evaluating safety of a certain treatment requires several phases. We wanted to take caution since this is the first study using eccentric overload exercise in PWH, and considering their severe state and the absence of flywheel experience, we decided that this was the proper first step before higher intensities and/or experimental studies can be conducted. Finally, future studies need to explore safety of eccentric overload exercise among PWH with a different degree arthropathy.

5 | CONCLUSIONS

A seated knee extension exercise performed with the flywheel at moderate intensity seems to be safe and is generally tolerated among severe PWH under adequate factor coverage. The flywheel variation provides higher eccentric rectus femoris activity at 60%-70% of the contraction cycle (breaking force moment) than the weight machine condition, while it provides lower eccentric muscle activity at the end of the contraction cycle.

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CONFLICT OF INTEREST

The authors report no conflict of interest.

AUTHOR CONTRIBUTIONS

JCL, SP-A, LLA and FQ conceived and designed the research study. JCL and SP-A recruited patients and collected the data. JCL, JJC, CCM and LLA analysed and interpreted the data. JCL wrote the paper. JCS, SB and FQ contributed essential reagents or tools. All authors reviewed and approved the final version of the paper.

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