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# Short-term effects of Pilates-based exercise on upper limb strength and function in people with Parkinson's disease



Helen Cristian Banks<sup>a</sup>, Thiago Lemos<sup>a</sup>, Laura Alice Santos Oliveira<sup>a</sup>, Arthur Sá Ferreira<sup>a,\*</sup>

<sup>a</sup> Postgraduate Program of Rehabilitation Sciences, Centro Universitário Augusto Motta/UNISUAM, Rio de Janeiro, RJ, Brazil

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# 1. Introduction

Parkinson's disease (PD) is a chronic and progressive neurologic disorder characterized by motor symptoms—bradykinesia combined with either rest tremor, rigidity, postural instability, and gait difficulty—that may result in functional impairments and recurrent falls, among other non-motor symptoms (Bloem et al., 2021). Determining the severity of PD can be challenging as the continuum between disease onset and advanced phases is highly variable in expression and rate of progression, with clinical instruments being used as a reliable categorical classification of mild, moderate, and severe PD (Martínez-Martín et al., 2015). PD provokes a significant decline in mobility and activities of daily living (Benka Wallén et al., 2015; Urell et al., 2021). It may result in a loss of independence and low adherence to engaging in regular exercise and physical activity, initiating a cycle of deconditioning and functional decline that compromises the health-related quality of

life (Ellis and Motl, 2013). Altogether, PD increases the risk of cardiovascular disease (Park et al., 2020). This, alongside the concomitant aging of the population (Li et al., 2019) and low levels of physical activity worldwide, highlights the need for rehabilitation programs that promote physical activity and lifestyle changes for this population (Benka Wallén et al., 2015; Bull et al., 2020).

People with PD show a 30–50% decrease in muscle strength when compared to healthy adults of the same age (Inkster et al., 2003; Kakinuma et al., 1998; Koller and Kase, 1986; Nocera et al., 2010; Schilling et al., 2009; Skinner et al., 2015; Stevens-Lapsley et al., 2012). In older adults, earlier studies report muscle weakness in different muscle groups including those of the upper limbs (UL) (Koller and Kase, 1986). The etiology of muscle weakness is still debatable and varies from a consequence of the characteristics of the disease to an intrinsic feature (Berardelli, 2001; Buckley and Hass, 2012; Cano-De-La-Cuerda et al., 2010; Corcos et al., 1996; David et al., 2012; Wichmann and DeLong,

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<sup>\*</sup> Corresponding author. Programa de Pós-graduação em Ciências da Reabilitação, Rua Dona Isabel 94, Bonsucesso, Rio de Janeiro, RJ, ZIP 21032-060, Brazil. *E-mail addresses:* thiago.lemos@souunisuam.com.br (T. Lemos), laura.oliveira@souunisuam.com.br (L.A.S. Oliveira), arthurde@souunisuam.com.br (A.S. Ferreira).

2007). Muscle weakness can compromise the functionality in PD, particularly in performing activities of daily living, and ultimately their quality of life; muscle weakness is a secondary cause of bradykinesia (Berardelli, 2001). It is also suggested that both muscle weakness and bradykinesia are involved in the mechanism of impaired dexterity (de Oliveira et al., 2008). Conversely, in large randomized clinical trials investigating different exercise interventions (e.g., multimodal training, progressive resistive training, and aerobic endurance training, among others), improvements in bradykinesia were reported (Mak et al., 2017). Also, finger strength training can improve dexterity in healthy older adults (Olafsdottir et al., 2008). Therefore, therapeutic approaches focused on UL muscle strength are relevant for this population (Ramazzina et al., 2017).

Rehabilitation programs for PD include exercises for improving gait (Pedersen et al., 1997), lower limb strength (Inkster et al., 2003), and balance training (Kamieniarz et al., 2021). Nonetheless, a systematic review including 13 high-quality randomized clinical trials highlighted the scarcity of studies investigating the effects of resistance training, performed against a resistance different from the body weight (Ramazzina et al., 2017). Rehabilitation programs using the Pilates method are emerging, focusing on the improvement of lower limb muscle strength and flexibility, dynamic and functional balance, reduction of the risk of falling, improvement of physical conditioning, quality of life, and postural stability (Cancela et al., 2018; Daneshmandi et al., 2017; Johnson et al., 2013; Mollinedo-Cardalda et al., 2018; Pandya et al., 2017; Suárez-Iglesias et al., 2019). However, there is no evidence regarding the feasibility and safety of Pilates-based exercises as a rehabilitation program to improve the UL muscle strength and functionality in people with PD. Because most Pilates exercises comprise bilateral coordination tasks-in which movements are controlled through a slow, precise muscle activation of major muscle groups-in which a hand grip is used to control the equipment, we hypothesized that such Pilates-based exercises may improve not only upper limb muscle strength but also bradykinesia and dexterity. Therefore, this study investigated the feasibility and safety of a Pilates-based exercise program in the treatment of UL to improve muscle strength, manual dexterity, bradykinesia, and functionality for people with PD.

# 2. Methods

# 2.1. Ethical aspects

This research protocol was developed according to the World Medical Association Declaration of Helsinki as revised in 2013 and the National Health Council No. 466/2012. The protocol was approved by the Institutional Ethics Research Committee of the Augusto Motta University Center (CEP/UNISUAM) before its execution (No. 39521220.9.0000.5235). Details of the study procedures were provided, and demographic data were collected of eligible individuals who agreed to participate after signing the informed consent form.

# 2.2. Study design and reporting

This was a feasibility and safety study (Hart and Bagiella, 2012) of an quasi-experimental (before-and-after) clinical trial. The exercise program was applied in individual sessions, 3 sessions per week lasting 30 min each, for 6 weeks.

This study followed the recommendations of sample sizes of clinical feasibility studies of interventions: 12 participants per intervention arm as a general rule (Julious, 2005); and 25, 15, or 10 participants for standardized effect sizes that are small (0.2), medium (0.5), or large (0.8), respectively (Whitehead et al., 2016). Hence, 15 participants were included in this study.

# 2.3. Setting and participants

Participants attending a private practice physiotherapy clinic were invited to participate in this study and other candidates were recruited through snowball sampling. The inclusion criteria comprised: the clinical diagnosis of PD confirmed by a neurologist; both genders; age between 50 and 80 years; mild to moderate motor impairment (at least stage 2 and at most 3 on the Hoehn and Yahr scale) (Hoehn and Yahr, 1967); minimum score of 18 on the Mini Mental State Examination (Almeida, 1998); no orthopedic, traumatic or rheumatologic disorders affecting upper limb function; no concomitant neurological disease; no deep brain stimulation; no uncontrolled cardiovascular disease (systolic blood pressure <180 mmHg and diastolic blood pressure <100 mmHg); and availability to attend the office for intervention sessions.

# 2.4. Feasibility and safety assessments

The viability of the program was assessed by the number of sessions the patient attended, the ability of each participant to perform the exercises, as well as the progressions of difficulty. Thus, attendance was recorded at each session, and each participant's performance of the exercises during the sessions was carefully observed. Safety was checked throughout the 18 program sessions by calculating the amount and type of adverse events such as abnormal pressure response to exercise (systolic >180 or diastolic >100 mmHg), prolonged fatigue or muscle soreness (up to 72 h after the session), syncope episodes, and the number of falls. For this purpose, participants were asked about adverse effects, BP was measured, and the number of adverse events was registered.

# 2.5. Baseline clinical assessments

Participants underwent anamnesis for evaluation of eligibility criteria, which included the application of the Movement Disorder Society - Unified Parkinson's disease Rating Scale (MDS-UPDRS) (Goetz et al., 2008) and the Hoehn and Yahr Scale (Hoehn and Yahr, 1967) for evaluation of the staging of the disease. Data regarding physical activity in the last 7 days was collected at baseline using the Portuguese-Brazil short-version (Matsudo et al., 2001; Mazo and Benedetti, 2010) of the International Physical Activity Questionnaire (IPAQ) Questionnaire and evaluated according to the frequency and duration of the activities. The participants were classified as *active* (vigorous activity  $\geq$ 3 days/week for >20 min/session; moderate physical activity >5 days/week for >30 min/session; or any activity >5 days/week and >150 min/week), irregularly active A (activity for  $\geq 5$  days/week or  $\geq 150$  min/week), *irregularly active B* (no adherence to frequency or duration criteria), or sedentary (no activity lasting  $\geq 10$  min/week) (Matsudo et al., 2001; Mazo and Benedetti, 2010).

# 2.6. Functional assessments

Participants underwent evaluation sessions before and after the rehabilitation program, focusing on UL muscle strength, manual dexterity, bradykinesia, and functionality. Before the intervention, the participants were instructed about each assessment and were allowed to practice once for familiarization with the procedures before data collection. To control for possible learning effects, after the intervention program the participants received the same instructions but did not perform a familiarization routine.

Muscle strength was assessed using the handgrip strength (HGS) measured with an analog dynamometer (Saehan model SH5001, Korea). The test was performed in the sitting position, with the shoulder of the arm to be tested adducted and the elbow flexed at 90°, with the forearm and wrist positioned in a neutral position. Participants performed three maximum isometric contractions for 3 s with both hands, with 1-min pause between measurements (Villafañe et al., 2016). The result of the test is the average of three measurements obtained by each hand.

Manual dexterity of the UL was assessed using the 9 Hole Peg Test (9HPT). The examiner briefly demonstrated the test and provided the following instructions to the participant: "Take the pins one at a time, using only the dominant hand, and place them in the holes, in any order, until all holes are filled; then remove the pins one at a time and return them to the container. Stabilize the frame with the holes with the non-dominant hand". The timer was started as soon as the individual touched the first pin and stopped when the last pin hit the container. The container was then placed on the opposite side of the board. The test was repeated in the same way for the non-dominant hand. Scores were evaluated separately for each hand (Mathiowetz et al., 1985).

Bradykinesia of the UL was assessed using the Movement Disorder Society – Unified Parkinson's Disease Rating Scale (MDS-UPDRS) part III. Specifically, we evaluated unilateral (Finger tapping; Hand movements; Pronation-supination movements) and global motor tasks (Arising from the chair; Global spontaneity of movement) separately. The MDS-UPDRS is a standard criterion to assess the clinical signs and symptoms of PD (Goetz et al., 2008) through self-reported and clinical observation by the examiner. Each item is scored from 0 to 4, with higher scores indicating greater impairment.

The functionality of the UL was assessed using the Test D'évaluation des Membres Supérieurs des Personnes Âgées (TEMPA) scale (Desrosiers et al., 1993). The Portuguese-Brazil version demonstrated excellent interrater agreement, test-retest reliability, and internal consistency (de Freitas et al., 2017). TEMPA comprises eight standardized tasks representative of daily living activities, including unilateral tasks (pick up and move a jar, pick up a pitcher and pour water into a glass, handle coins, pick up and move small objects) and bilateral tasks (open a jar and take out a spoonful of coffee, unlock a lock and open a pill container, write on an envelope and stick on a stamp, shuffle and deal playing cards) using a range of real objects. These tasks are assessed through both quantitative (execution speed quotation) and qualitative (functional and task analysis score) dimensions. Each TEMPA tasks was demonstrated, briefly trained, and then the test was performed and timed. The tasks were timed individually, and the total score represents the sum of these dimensions, with higher values corresponding to greater disabilities.

# 2.7. Intervention: pilates-based exercises for upper limb

Full descriptions and illustrations of the Pilates-based rehabilitation program are shown in Supplementary File 1; a summary of the exercises and their progression is shown in Supplementary File 2. Briefly, the rehabilitation program consisted of 18 exercises using Pilate's equipment-namely Reformer (10 exercises), Cadillac (4 exercises), Barrel (2 exercises), and Chair (2 exercises)-in approximately 30-min sessions, twice a week, for 6 weeks. As part of the warm-up, static stretching of the shoulder muscles was performed 3 times for 20 s each using the Cadillac bars before and after each session. The session was not interrupted though if the patient required additional time to recover or to complete the exercises. All the strengthening exercises were performed in 2 sets of 10 repetitions each, with a 2-min interval between sets. The circuit of exercises shown in Supplementary File 2 was designed to impose progressively additional effort when performing the selected exercises, through the recruitment of more (or larger) muscle groups under an increased cognitive/coordination demand to use Pilate's equipment. Also, an increase in the spring load of the equipment was made according to the Borg scale.

# 2.8. Study outcomes

The study outcomes comprised UL and muscle strength (HGS) (Villafañe et al., 2016), motor dexterity (9HPT task time) (Mathiowetz et al., 1985), bradykinesia (MDS-UPDRS scores) (Goetz et al., 2008), and functionality (TEMPA task time) (de Freitas et al., 2017; Desrosiers et al., 1993).

# 2.9. Statistical analysis

Statistical analysis was performed using JASP v. 0.16.2 (https://jaspstats.org) and R software version 4.2.1 (https://www.r-project.org). The normality of distribution was checked using the Shapiro-Wilk Test. Descriptive data are shown as median [interquartile range] or absolute (relative) frequency for continuous and categorical variables, respectively. Within-group comparisons (before and after) were conducted using the Wilcoxon signed-rank test. The effect size was estimated by calculating the rank-biserial correlation. As a feasibility study, evidence of statistical significance was set at p < 0.10 given that such studies are not designed to observe 'positive results' but to guide future, large studies (Arain et al., 2010; Lakens et al., 2018). P-values were adjusted for each outcome (HGS, 9HPT, TEMPA, MDS-UPDRS) using the false-discovery rate method to account for multiple comparisons.

# 3. Results

A total of 23 participants were contacted for assessment of the eligibility criteria; of these, 3 were excluded due to age; 2 did not reach the minimum score on the MMSE; 2 were unable to attend the research site; 1 had orthopedic and rheumatologic alterations that prevented them from performing exercises with the upper limbs. Adherence to the 18 Pilates sessions was 100% among the 15 patients who completed the trial.

Table 1 shows the characteristics of the 15 participants who completed the protocol. They were predominantly men (n = 11, 73%), older adults (66 [9] years), right-handed (n = 15, 100%), overweight (n = 7, 47%; body mass index of 27.6 [5.4] kg/m<sup>2</sup>), and irregularly active (n = 8, 53%). The time since PD diagnosis was 4 [4] years, and the staging of PD according to the Hoehn and Yahr Scale was mild to moderate (Stage 2: n = 11, 73%; 2.0 [0.3] points). All participants performed the exercises as proposed, and the only adverse event observed was mild muscle pain.

Table 2 shows the within-group comparison of the functional outcomes of the study. After adjusting the p-value for family-wise multiple comparisons, evidence of statistical significance was retained only for bradykinesia (global spontaneity of movement; adjusted p = 0.048). No

#### Table 1

Characteristics of the studied sample (n = 15).

Variable	Values
Sex, Women:Men, n (%)	4:11 (27:73)
Age, years median [IQR]	66 [9]
Anthropometry, median [IQR]	
Body height, m	1.67 [0.06]
Body mass, kg	79.0 [21.3]
Body mass index, kg/m <sup>2</sup>	27.6 [5.4]
Nutritional status, n (%)	
Eutrophic	5 (33)
Overweight	7 (47)
Obese I	1 (7)
Obese II	2 (13)
Dominance, right body side, n (%)	15 (100)
Time since diagnosis, years median [IQR]	4 [4]
Hoehn & Yahr, median [IQR]	2.0 [0.3]
Stage 2, n(%)	11 (73)
Stage 2.5, n(%)	4 (27)
Mini Mental State Exam median [IQR]	29 [3.5]
Physical activity <sup>a</sup> , n (%)	
Active	6 (40)
Irregularly active A	3 (20)
Irregularly active B	5 (33)
Sedentary	1 (7)

<sup>a</sup> Active: vigorous activity  $\geq 3$  days/week for  $\geq 20$  min/session; moderate physical activity  $\geq 5$  days/week for  $\geq 30$  min/session; or any activity  $\geq 5$  days/week and  $\geq 150$  min/week. Irregularly active A: activity for  $\geq 5$  days/week or  $\geq 150$  min/week. Irregularly active B: no adherence to frequency or duration criteria. Sedentary: no activity lasting  $\geq 10$  min/week.

#### Table 2

Within-group	comparison	of the study	outcomes	(n =	15	)
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Variable	Before	After	Adjusted* P-values	Rank-biserial correlation [95%CI]
HGS, kgf				
Dominant side	26.6	27.0	0.394	-0.258 [-0.686;
	[13.0]	[12.2]		0.301]
Nondominant side	29.3	24.3	0.394	-0.314 [-0.726;
	[10.7]	[16.6]		0.263]
9HPT, s				
Right	28.0	29.0	0.728	-0.114 [-0.610;
	[12.5]	[10.5]		0.446]
Left	28.0	33.0	0.554	-0.352 [-0.735;
	[13.5]	[16.6]		0.244]
TEMPA, s				
Bilateral tasks				
Open a jar and take out	14.0	13.0	0.350	0.343 [-0.233;
a spoonful of coffee	[7.0]	[4.5]		0.741]
Unlock a lock and	23.0	22.0	0.338	0.400 [-0.169;
open a pill container	[13.0]	[8.0]		0.769]
Write on an envelope	33.0	22.0	0.338	0.442 [-0.101;
and stick on a stamp	[16/0]	[14.5]		0.782]
Shuffle and deal	29.0	24.0	0.338	0.467 [-0.069;
playing cards	[13.0]	[17.0]		0.794]
Pick up and move a	6.0	5.0	0.338	0.556 [-0.150;
jar	[2.0]	[1.0]		0.886]
Unilateral tasks				
Pick up and move a	5.0	5.0	0.338	0.489 [-0.198;
jar (left)	[1.0]	[2.5]	0.050	0.854]
Pick up a pitcher and	7.0	7.0	0.350	0.341 [-0.256;
pour water into a	[3.5]	[3.0]		0.749]
glass (right)	0.0	7.0	0.250	0.205 [ 0.200
Pick up a pitcher and	9.0	7.0	0.350	0.385 [-0.208;
pour water into a glass (left)	[4.5]	[4.5]		0.771]
Handle coins (right)	17.0	15.0	0.338	0 420 5 0 124
Handle Collis (Hgilt)	[4.5]	[4.0]	0.338	0.438 [-0.124; 0.787]
Handle coins (left)	20.0	19.0	0.787	0.136 [-0.486;
Handle coms (ieit)	[7.0]	[6.5]	0.707	0.667]
Pick up and move	22.0	21.0	1.000	-0.010 [-0.526;
small objects (right)	[6.0]	[11.0]	1.000	0.540]
Pick up and move	26.0	20.0	0.144	0.742 [0.362;
small objects (left)	[13.5]	[7.0]	01111	0.910]
MDS-UPDRS, score	[10:0]	[,10]		01910]
Bilateral tasks				
Arising from chair	0.0	0.0	1.000	1.000 [ 1.000;
0	[1.0]	[0.5]		1.000]
Global spontaneity of	1.0	0.0	0.048	1.000 [ 1.000;
movement	[0.0]	[1.0]		1.000]
Unilateral tasks				-
Finger tapping	0.0	0.0	0.199	1.000 [ 1.000;
(right)	[1.0]	[1.0]		1.000]
Finger tapping (left)	1.0	0.0	0.199	1.000 [ 1.000;
	[1.0]	[1.0]		1.000]
Hand movements	0.0	0.0	0.199	1.000 [ 1.000;
(right)	[1.0]	[0.5]		1.000]
Hand movements	0.0	0.0	0.199	1.000 [ 1.000;
(left)	[1.0]	[1.0]		1.000]
Pronation-	0.0	0.0	0.199	1.000 [ 1.000;
supination	[1.0]	[0.5]		1.000]
movements (right)				
Pronation-	0.0	0.0	0.395	1.000 [ 1.000;
supination	[1.0]	[0.0]		1.000]
movements (left)				

HGS: handgrip strength. 9HPT: 9 Hole Peg Test. TEMPA: Test D'évaluation des Membres Supérieurs des Personnes Âgées scale. MDS-UPDRS: Movement Disorder Society – Unified Parkinson's disease Rating Scale. Descriptive summaries are shown as median [interquartile range]. \*P values are adjusted for multiple comparisons using the false discovery rate method. statistical evidence of a difference was observed for UL muscle strength (HGS) or motor coordination (9HPT).

# 4. Discussion

This study aimed to investigate the feasibility and safety of a Pilatesbased exercise program for treating UL to enhance muscle strength, manual dexterity, bradykinesia, and functionality in people with PD. Major strengths of this study include using standard, valid, and reliable methods for assessment of the UL outcomes (Desrosiers et al., 1993; Langston et al., 1992; Mathiowetz et al., 1985; Villafañe et al., 2016), therefore extending its external validity and application to a clinical context.

This study is the first to provide evidence regarding Pilates-based exercises as a rehabilitation program to improve UL motor coordination in people with PD. Previous studies showed that Pilates-based rehabilitation programs may enhance physical conditioning and quality of life (Cancela et al., 2018), strengthen of the lower limbs (Mollinedo-Cardalda et al., 2018), and improve postural control, postural balance, and risk of falling (Daneshmandi et al., 2017; Johnson et al., 2013: Mollinedo-Cardalda et al., 2018: Pandva et al., 2017). The loss of strength and mobility can substantially affect the functionality in performing activities of daily living, leading to a gradual loss of independence and compromising their quality of life (Ramazzina et al., 2017). People with PD have significant muscle weakness (Koller and Kase, 1986), needing a longer time of intervention for a possible gain in muscle strength, which also applies to fine motor coordination. The Pilates method's equipment offers options for resisted exercises using springs, offering a systematic approach to enhancing muscle strength.

The main findings of this study suggest that the Pilates-based exercise program for the treatment of UL motor coordination is feasible and safe for this population. We can hypothesize that outcomes related to functionality and bradykinesia could be improved by the mobility that the method provides through the amplitude of movement added to the resistance of the equipment springs (Suárez-Iglesias et al., 2019). We opted not to delve into an in-depth discussion about these findings because the applied study design lacks strong control of rival hypotheses about the effects of the intervention. 'Negative' results, particularly in this case, should not be interpreted as 'absence of evidence' (Altman and Bland, 1995). The observed pre-post changes in UL bradykinesia require further investigation in large, randomized clinical trials.

Older people with PD are more exposed to an increased risk of cardiovascular disease and low levels of physical activity worldwide. Muscle strength exercises are increasingly acknowledged as a nonpharmacological therapeutic option for preventing and managing chronic conditions, including cardiovascular diseases, both in the general population (Artero et al., 2012) and in people with PD (Uhrbrand et al., 2015). Recent studies also showed an inverse association of muscle strength (including upper limb measurements) with central and peripheral cardiovascular function (Alomari et al., 2020; Alomari et al., 2017). Considering the potential of Pilates-based exercises to enhance physical conditioning (Cancela et al., 2018; Daneshmandi et al., 2017; Johnson et al., 2013; Mollinedo-Cardalda et al., 2018; Pandya et al., 2017; Suárez-Iglesias et al., 2019), our findings also encourage further investigation about the potential of the Pilates-based exercise program to promote physical activity and foster long-term, sustained lifestyle changes for this population.

# 4.1. Limitations

Some limitations and strengths are worth discussing. A major threat to the interval validity comprises a rival hypothesis in which changes in UL bradykinesia were not the results of the Pilates-based rehabilitation protocol but some other event. However, this is not likely as the participants were not systematically exposed to changes in other major interventions (e.g., medications). The large age range of the sample also may have affected the pooled summaries of the sample's functional assessments, which should be accounted for in future studies. As for the external validity, our findings must be interpreted with caution, particularly in populations other than older adults with PD. Also, we acknowledge the large number of family-wise multiple comparisons performed here that, despite being handled by adjusting p-values, it is not advisable for explanatory studies (Althouse, 2016) as it may conversely increase the type-II error rate. Finally, as a feasibility study, the observed results must be considered preliminary, and further confirmation with randomized clinical trials is warranted before introducing this program in regular physiotherapy sessions.

#### 5. Conclusions

Short-term Pilates-based exercise program in the treatment of upper limb muscle strength, manual dexterity, bradykinesia, and functionality is both feasible and safe for people with PD. The observed changes in upper limb bradykinesia warrant further investigation through randomized clinical trials.

# Author declaration

We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order of authors listed in the manuscript has been approved by all of us.

We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing of publication, with respect to intellectual property. In so doing we confirm that we have followed the regulations of our institutions concerning intellectual property.

We further confirm that any aspect of the work covered in this manuscript that has involved human patients has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript.

We understand that the Corresponding Author is the sole contact for the Editorial process (including Editorial Manager and direct communications with the office). He is responsible for communicating with the other authors about progress, submissions of revisions and final approval of proofs. We confirm that we have provided a current, correct email address which is accessible by the Corresponding Author and which has been configured to accept email from arthur sf@icloud.com.

# CRediT authorship contribution statement

Helen Cristian Banks: Data curation, Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing. Thiago Lemos: Conceptualization, Methodology, Writing – review & editing. Laura Alice Santos Oliveira: Conceptualization, Methodology, Writing – review & editing. Arthur Sá Ferreira: Conceptualization, Formal analysis, Funding acquisition, Methodology, Project administration, Software, Supervision, Visualization, Writing – original draft, Writing – review & editing.

# Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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# Appendix A. Supplementary data

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