



# The effects of running a 12-km race on neuromuscular performance measures in recreationally competitive runners

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## ABSTRACT

**Background:** The number of individuals participating in organised races is increasing, with few studies undertaken in ecologically-valid settings. Running involves cyclical movements and activation of lower-extremity muscles, with fatigue and foot-strike pattern proposed as factors contributing to running-related injuries.

**Research question:** Our aim was to investigate the effects of running a 12-km race on plantar pressure distribution, postural balance, foot-strike pattern, and plantar-flexion strength. A secondary aim was to compare actual versus anticipated race finishing times and foot-strike patterns.

**Methods:** Twenty-four recreationally competitive runners (15 males, 9 females) completed the following tests immediately before and after a 12-km race: (1) plantar pressure distribution in self-selected bilateral stance; (2) 30-seconds eyes-closed feet-together postural balance; (3) running foot-strike angle; and (4) peak plantar-flexion isometric force. In-race foot-strike angle and patterns were also assessed at 3 and 10 km.

**Results:** Post-race left and right foot plantar pressure distribution, postural balance, and plantar-flexion force measures significantly differed from pre-race measures. These changes were associated with small to large standardised effects (absolute ES: 0.42 to 0.94). On average, the relative pressure under the left foot decreased by  $3.2 \pm 5.0\%$ ; the centre of pressure path length and area of the 95th percentile ellipse from the balance test increased by  $5.7 \pm 8.9$  cm and  $18.2 \pm 21.3$  cm<sup>2</sup>; and peak plantar-flexion isometric force decreased by  $0.23 \pm 0.28$  times body weight. Participants predicted their finishing times relatively well, but not their foot-strike patterns. No meaningful change in foot-strike angle or pattern was observed pre- to post-race, or between 3 and 10 km.

**Significance:** Running a 12-km race influenced neuromuscular measures, confirming racing-induced fatigue in our recreationally competitive runners. However, these alterations did not lead to observable changes in foot-strike pattern, indicating that this measure might not be appropriate for quantifying fatigue in recreationally competitive runners.

## 1. Introduction

Mass participation in running is positive given its many health-enhancing benefits, including decreased risk of all-cause mortality [22]. However, running involves repetitive impacts, with injury incidence sourced from a literature review reported to range from 19.4 to 79.3% across 12 to 32 weeks [34]. Foot-strike pattern and fatigue are two of the risk factors linked with an increased likelihood of lower-extremity running injuries [6], and are topics of frequent clinical and scientific inquiry. Foot-strike pattern, for instance, has been associated with different biomechanical characteristics [1] and increased likelihood of certain types of running injuries, with ankle and foot injuries more frequent in fore-foot strikers, and hip and knee injuries more prevalent

in rear-foot strikers [6].

Neuromuscular fatigue from sustained exercise results in quantifiable declines in performance, such as reductions in maximal force or power [25]. With fatigue of select lower-extremity muscles, workload shifts to less fatigued muscles and kinematic adaptations occur to maintain performance levels and moderate impact forces [19]. However, with a decreased ability of the musculoskeletal system to attenuate impact forces, the risk of injury increases [26]. Running has also been linked to decreased plantar-flexor muscle activation [29], alterations in plantar pressure loads [24], and balance impairments [37], with running eliciting greater balance impairments than cycling presumably due to more selective fatigue of muscles involved with upright stance and locomotion [37].

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Self-reporting of information is often used in practice and research, for instance, to record injury incidence or experience level. Amongst runners, the most commonly self-reported foot-strike pattern is mid-foot [2], with a large proportion of mid-foot and fore-foot runners changing to rear-foot during a marathon [21]. However, self-reported foot-strike pattern accuracy is relatively low, with agreement levels reported to range from 43.5 to 68.3% [2,11]. Running experience potentially contributes to errors in self-reported patterns, as collegiate runners have demonstrated a 13% higher self-reported accuracy compared to recreational runners [2]. Likewise, more experienced runners are better able to accurately predict their race finishing times and regulate pace [23].

Running a race often results in an increased running pace. A sudden change in running pace may lead to the development of running-related injuries [28], with a superior ability to regulate race pace linked with blood markers indicating muscle breakdown [7]. In a study by Taunton et al. [31], 18.2% of runners self-reported at least one new lower-extremity injury due to marathon participation. These running injuries might have resulted from an increased pace, racing-induced fatigue, or suboptimal awareness of one's running ability; hence the interest in assessing how well runners can predict their race finishing times in the context of fatigue and injury prevention.

Determining any shifts in plantar pressure load, balance ability, foot-strike, and force production due to running-induced fatigue may provide insights into appropriate injury prevention and pre-conditioning strategies. Most of the existing literature is laboratory and treadmill based. While such studies contribute to our knowledge, most running occurs outside of laboratory environments. Our aims were to investigate the effect of running a 12-km race on plantar pressure distribution, postural balance, foot-strike pattern and angle, and plantar-flexion strength in recreationally competitive runners. We anticipated increases in the relative posterior plantar pressure loads, declines in postural balance measures, an increase in rear-foot strike patterns and angles, and impairments in plantar-flexion strength subsequent the 12-km race. A secondary aim was to compare expected to actual race finishing times and foot-strike patterns to explore the accuracy of self-reported outcomes and 12-km race predictions.

## 2. Material and methods

### 2.1. Participants

Twenty-four recreationally competitive runners (15 males, 9 females, Table 1) volunteered and provided written informed consent prior to participation. Inclusion criteria were  $\geq 18$  years, free from musculoskeletal or neurological conditions, and anticipated 12-km times of 75 min or less (pace  $\leq 6:15/\text{km}$ ). Participants were recruited via e-newsletters sent by the race organisers, and pamphlets handed out on race day. The protocol was approved by the Human Research Ethics Committee of the University of Waikato [HREC(Health)#11] and

**Table 1**

Participant and shoe characteristics. Values are means  $\pm$  standard deviations and medians (1st quartile, 3rd quartile).

	Male (n = 15)	Female (n = 9)	Total (n = 24)
<b>Participant</b>			
Age (years)	39.4 $\pm$ 11.2	31.5 $\pm$ 7.57	36.5 $\pm$ 11.2
Height (cm)	176.2 $\pm$ 6.2	164.3 $\pm$ 6.4	171.6 $\pm$ 8.5
Body mass (kg)	81.1 $\pm$ 8.0	60.6 $\pm$ 6.5	73.6 $\pm$ 12.5
Runs (per week)	3 (3, 5)	3 (3, 4)	3 (3, 5)
Running experience (years)	6 (2, 12)	5 (2, 10)	5 (2, 10)
<b>Shoe</b>			
Mass (g)	306.5 $\pm$ 29.5	251.5 $\pm$ 35.1	283.3 $\pm$ 41.7
Heel height (mm)	28.0 $\pm$ 6.0	26.8 $\pm$ 6.2	27.5 $\pm$ 6.0
Heel-to-toe drop (mm)	9.8 $\pm$ 2.0	9.7 $\pm$ 1.3	9.8 $\pm$ 1.7

complied with the Declaration of Helsinki. Given the on-field nature of the experiment, no sample size computations were performed a priori. As many runners as possible were recruited and tested on race day.

Participants completed a baseline questionnaire pre-race that included self-reported foot-strike (rear-foot, mid-foot, or fore-foot) and expected race times. Participants were familiarised with the testing procedures and each apparatus was zeroed before every trial. Plantar pressure distribution, postural balance, foot-strike pattern, and plantar-flexion isometric strength were tested sequentially, with participants wearing their own running shoes. Immediately post-race (typically within 2 min), the same tests were performed. Participants median ratings of perceived exertion post-race on a 20-point Borg's scale was 17 (interquartile range: 15–18). The actual 12-km times of participants were obtained from the official race results.

### 2.2. Plantar pressure distribution

Plantar pressure was assessed using the Footscan® entry-level USB2 platform (150 Hz frequency) and Gait 7 software (RScan International, Belgium). Participants stood in the middle of the platform and walked in place for a few seconds before stopping in a self-selected comfortable, usual stance position [18], remaining still and looking straight ahead with arms by their side. Once in a stable position, static plantar pressure in standing was recorded per the manufacturer's recommendations and used to extract the relative pressure (%) distributed into anterior-posterior and left-right areas. The reported reliability of these measures between session is high, with intra-class correlation coefficient (ICC) values ranging from 0.948 to 0.968 and the percentage error ranging from 3.3 to 5.9% [33].

### 2.3. Postural balance

Postural balance was assessed using an AMTI AccuGait Optimized forceplate sampling at 150 Hz and Balance Clinic software v.2.03.00 (Advanced Mechanical Technology Incorporated, Watertown, MA). Participants stood in the middle of the forceplate, feet together, arms by their side, and as still as possible with their eyes closed. Once in the designated position for 3 s, 30 s of data were recorded and used to extract centre of pressure path length (COP<sub>path</sub>, cm) and area of the 95<sup>th</sup> percentile ellipse (COP<sub>area95</sub>, cm<sup>2</sup>). Using a similar postural balance test (but barefoot), Bauer et al. [3] found acceptable reliability of these measures, with corresponding ICC values of 0.945 and 0.710.

### 2.4. Pre- and post-race foot-strike pattern and angle

Foot-strike pattern and angle pre-race and post-race was assessed on 15-m of level asphalt using a digital camera (Cyber-shot DSC-RX10 II, Sony, Tokyo, Japan) sampling at 240 Hz on a 1-m high tripod, 6-m away from and to the right of participants. Participants ran at their perceived race pace through the 15-m area three times pre-race (4.3  $\pm$  0.5 m/s) and post-race (4.2  $\pm$  0.6 m/s, paired *t*-test *P* = 0.2024), with a 30 s walking rest between trials. The Siliconcoach Pro 8 software (The Tarn Group, Dunedin) was used to extract foot-strike pattern and angle from the right foot-strike occurring nearest to the middle of the 15-m runway. Foot-strike pattern was classified based on which part of the foot made ground contact with the ground first as rear-foot (heel or rear third of the sole only), mid-foot (mid-foot or entire sole), or fore-foot (fore-foot or front half of the sole) as described by Hasegawa et al. [12]. Foot-strike angles were measured as the line joining the sole of the shoe from the point of first contact and the horizontal plane, where positive and negative angles represent more pronounced rear-foot and fore-foot strikes. The average foot-strike angle and most common pattern from the three trials pre-race and post-race was used for analyses. Within and between raters, foot-strike pattern agreement (99.4%,  $\kappa$  = 0.96) and foot-strike angle (ICC = 0.88) exhibit high reliability, with a typical error of measure of 2.5° for

**Table 2**

Postural balance, plantar pressure distribution, plantar-flexor strength, and foot-strike angle measures pre and post 12-km organised race ( $n = 24$ ). Values are means  $\pm$  standard deviations. The magnitudes of clear effects are reported.

	Pre	Post	Change	ES [90% CI]	MBI
<b>Balance (<math>n = 23</math>)</b>					
COP <sub>path</sub> (cm)	80.5 $\pm$ 19.0	98.8 $\pm$ 25.7	18.2 $\pm$ 21.3	0.85 [0.53, 1.17]	large*
COP <sub>area95</sub> (cm <sup>2</sup> )	6.2 $\pm$ 3.2	11.9 $\pm$ 10.4	5.7 $\pm$ 8.9	0.94 [0.58, 1.29]	large*
<b>Plantar pressure</b>					
Anterior (%)	52.3 $\pm$ 6.9	54.2 $\pm$ 7.0	1.9 $\pm$ 5.0	0.25 [-0.01, 0.50]	unclear
Posterior (%)	47.7 $\pm$ 6.9	45.8 $\pm$ 7.0	-1.9 $\pm$ 5.0	-0.28 [-0.52, -0.04]	unclear
Left (%)	55.2 $\pm$ 5.5	52.0 $\pm$ 5.0	-3.2 $\pm$ 5.0	-0.58 [-0.90, -0.26]	small <sup>f</sup>
Right (%)	44.8 $\pm$ 5.5	48.0 $\pm$ 4.9	3.2 $\pm$ 5.0	0.55 [0.25, 0.85]	small <sup>f</sup>
<b>Plantar-flexion strength (<math>n = 22</math>)</b>					
Force (BW)	2.13 $\pm$ 0.55	1.90 $\pm$ 0.43	-0.23 $\pm$ 0.28	-0.42 [-0.60, -0.24]	small <sup>f</sup>
<b>Foot-strike</b>					
Angle (°)	16.7 $\pm$ 6.1	17.2 $\pm$ 5.0	0.5 $\pm$ 4.3	0.10 [-0.13, 0.33]	trivial

Abbreviations: CI, confidence interval; ES, effect size; MBI, magnitude-based inference.

\* Paired *t*-test  $P < 0.05$ . An effect size was clear when its 90% confidence interval did not overlap the thresholds for small positive and small negative effects.

foot-strike angle [27].

### 2.5. In-race foot-strike pattern and angle

In-race foot-strike patterns and angles were investigated in vicinity of the 3 and 10 km on level asphalted sections of the 12 km race. A digital camera (Cyber-shot DSC-RX10 II, Sony, Tokyo, Japan) was mounted on a 1-m high tripod 3.5-m away from the road (approximately 6-m from the main running area) to the right side of runners. A frequency of 120 Hz was used to allow continuous recording. Identification numbers were written with permanent markers on participants' right legs for identification purposes.

### 2.6. Plantar-flexion strength

To assess plantar-flexion strength, participants stood on two dual-axis forceplates (PASCO, Roseville, CA) sampling at 500 Hz positioned under a squat rack. Participants pushed as hard as possible upwards against a 20-kg Olympic barbell for 10 s using their calf muscles to exert force into the ground, keeping their knees straight. The task was an isometric bilateral heel-raise task as the barbell was pushed against two safety bars. The height of the barbell was standardised to allow the bar to rest on participants' shoulders while allowing a slight heel lift from the ground during the exertional task. Participants warmed-up for the maximal trial by completing 50 and 70% maximal effort trials. The PASCO Capstone Software v.1.4 was used to extract peak force normalised to body weight (% BW) from the 10-s maximal trial. Test-retest reliability data from three trials conducted in our laboratory ( $n = 66$  male and female participants) indicate high reliability of this measure (ICC = 0.91, coefficient of variation = 5.1%).

Due to time constraints and on-field experimental nature of our study, one trial was conducted for all tests after the initial familiarisation with all measurements, except for the running trials where typical performance across three trials was extracted. Due to the eminent race start, two participants did not complete the plantar-flexion test. In addition, one participant's balance data did not record correctly. Hence, pre- and post- race comparisons for these particular measures are from 22 and 23 participants, respectively.

### 2.7. Statistical analysis

Means, standard deviations (SD), medians, and interquartile ranges (IQR) were computed to describe the data. A customisable statistical spreadsheet and between-participant pre-race SD were used to compute effect sizes (ES) [16]. The smallest worthwhile difference in means was set to 0.20 of these SDs, except for foot-strike angle where it was set to

2.5° based on prior test-retest data [27]. Magnitudes of the ES were interpreted as trivial (ES < 0.2), small (0.2  $\leq$  ES < 0.6), moderate (0.6  $\leq$  ES < 1.2), and large (ES  $\geq$  1.2), and deemed clear if their 90% confidence interval [lower, upper] did not overlap thresholds for small positive and small negative effects. Variables were log-transformed to reduce bias arising from non-uniformity of error and used for interpreting all statistical comparisons, except for foot-strike angle where log-transformation was not appropriate. Statistical significance from paired *t*-tests was set at  $P < 0.05$ . The 3-km and 10-km foot-strike angles were compared using the same statistical approaches. Levels of agreement and 90% confidence intervals between pre-race and post-race, 3-km and 10-km, and perceived and actual foot-strike patterns were computed using the Wilson score method incorporating continuity correction [9].

## 3. Results

Participants completed the 12-km race in 61  $\pm$  8 min, which was significantly faster than their anticipated times of 63  $\pm$  9 min ( $-2 \pm 4$  min,  $P = 0.0426$ ). However, this latter difference was trivial based on the ES ( $-0.15$  [-0.28, -0.02]).

### 3.1. Pre versus post 12-km race

There were clear and significant changes in most measures post-race, except for anterior and posterior plantar pressure distribution and foot-strike angle measures (Table 2). Changes in both balance variables (COP<sub>path</sub> and COP<sub>area95</sub>) were associated with a large ES, whilst the ES related to the change in plantar pressure distribution and plantar-flexor strength was moderate and small, respectively. Changes in foot-strike angle from pre-race (16.7  $\pm$  6.1°) to post-race (17.2  $\pm$  5.0°) were trivial, with all participants classified as rear-foot across observations.

### 3.2. 3-km versus 10-km

No significant difference ( $P = 0.5703$ ) in foot-strike angle was observed between the 3-km (9.9  $\pm$  4.9°) and 10-km (10.6  $\pm$  3.1°) marks, with the mean change of 0.7  $\pm$  4.3° being clearly trivial (ES: 0.14 [-0.15, 0.43]). All participants were rear-foot strikers at both points, except for one runner who changed from mid-foot to rear-foot (agreement: 95.8% [80.4, 99.7]).

### 3.3. Expected versus actual foot-strike pattern

All 24 participants were rear-foot strikers based on pre-, post-, and in-race measures. Only 13 participants correctly identified their rear-

foot pattern (54.2% [36.0, 71.4]). The remaining self-reported a mid-foot and fore-foot pattern in 8 and 3 instances, respectively.

#### 4. Discussion

Running a 12-km race resulted in observable changes in postural balance ( $COP_{path}$  and  $COP_{area95}$ ), left-and-right plantar pressure distribution, and plantar-flexion isometric strength. These neuromuscular changes suggest racing-induced fatigue in our recreationally competitive runners, corroborate the importance of plantar-flexion strength in racing, and that postural control is altered in fatigued runners. Despite quantifiable declines in postural balance and plantar-flexion strength, self-selected foot-strike angle did not meaningfully change and might not be an appropriate indicator of fatigue in runners, particularly in habitual rear-foot strikers.

##### 4.1. Plantar pressure distribution

Previous research has shown that a greater proportion of runners rear-foot strike at 32 km of a marathon compared to 10 km [21], and that running-induced fatigue decreases plantar pressure loads at the toes [24]. We hence expected an increase in the relative posterior plantar pressure load supporting these reported changes towards a more rear-foot strike and decreased toe pressure. The lack of significant anterior-to-posterior change in plantar pressure distribution in our study might have several explanations, including that all our participants were rear-foot strikers and demonstrated comparable foot-strike angles pre- and post-race and at the 3-km and 10-km mark of the race. Furthermore, the plantar pressure distribution was taken under a static condition rather than a dynamic one.

We did observe a meaningful decrease in the relative plantar pressure distributed under the left foot of our runners of  $3.2 \pm 5.0\%$ . The shift observed from left to right could potentially reflect compensatory strategies of muscles in redistributing workloads to less fatigued muscles or the influence of running on a cambered road [32]. These findings somewhat contrast with a previous study conducted on experienced recreational marathoners [15] where no significant changes in peak or mean plantar pressure between the dominant and non-dominant feet were observed between pre-race, in-race, and post-race measures, although the dominant foot was favoured throughout the race. We did not seek information relating to foot dominance or quantified average and peak plantar loads; hence, direct comparisons with this previous study is challenging [15].

##### 4.2. Postural balance

Postural balance measures worsened following the 12-km race in our runners, with large and significant increases in both  $COP_{path}$  and  $COP_{area95}$ . A review of the literature on postural control highlights how balance impairments post-exercise are likely of multi-factorial origin, and can result from fatigue, hyperventilation, functional deterioration of mechanoreceptors and proprioceptors, dehydration, and hyperthermia [37]. Previous studies involving exhaustive running [8,35] corroborate deterioration in postural stability, with larger impairments in eyes-closed rather than eyes-open conditions [8]. Although investigating the time-course of impairments was not within the scope of our study, postural impairments subsequent to aerobic and anaerobic exercise protocols have been shown to return to baseline values within thirteen minutes [10].

##### 4.3. Foot-strike pattern

Our runners were rear-foot strikers in all but one 3-km observation, with no meaningful change in self-selected foot-strike angle between pre-race and post-race measures or 3-km and 10-km measures. Two prior fatiguing studies observed a decrease in dorsiflexion angle at

initial ground contact whilst running on a treadmill [5,19], resulting in a greater area of the heel contacting the ground. Such changes were not readily observed in our population, which might be due to the on-field nature of our experiment and 2D as opposed to 3D methods used to quantify foot-strike angle.

Although not statistically compared, foot-strike angles were apparently less acute in-race ( $10.3 \pm 3.5^\circ$ ) than out-of-race ( $17.0 \pm 5.1^\circ$ ). While the difference could be due to running speed, average in-race speed (3.28 m/s) was slower than what was recorded pre- and post-race (4.25 m/s); hence, our change in foot-strike angle is opposite to findings of increasing mid-foot or fore-foot strike at faster self-selected running speeds [4]. A more plausible explanation to the difference between in-race and out-of-race foot-strike angles could be the data capture under semi-controlled conditions with an evident examiner versus natural conditions with no clear knowledge of examination. Testing devices have the potential to alter running gait, with differences in hip and ankle kinematics observed between running over an embedded forceplate, two different types of plantar pressure mats, and no force-measuring device [30]. Specifically, ankle plantar-flexion was significantly greater when running over plantar pressure mats compared to no device, with an embedded forceplate causing the least deviation from uninhibited running [30]. These findings suggest that running gait is altered when participants are aware of force-sensing measurement devices, which might extend to awareness of being recorded.

##### 4.4. Perceived versus actual foot-strike pattern

A little over half of our participants accurately predicted their foot-strike pattern. Our results are similar to the treadmill-based results from Bade et al. [2] where 43.5% of recreational runners correctly identified their foot-strike patterns compared to patterns determined using reflective markers placed on shoes. Goss et al. [11] found that self-reported foot-strike pattern was accurate in 68.3% of cases using a similar foot-strike pattern identification procedure to ours. Their use of two (rear-foot and anterior foot-strike) compared to the three foot-strike patterns can partly explain their superior accuracy. Overall, these data confirm that self-assessment of foot-strike pattern by runners is subject to error and requires objective quantification for valid inferences.

##### 4.5. Perceived versus actual running performance

Our participants were able to predict their finishing times relatively well compared to other research [17], which could be due to most participants running three times per week and having five years of running experience, despite considering themselves as “recreational” runners. Our inclusion criteria included an anticipated 12-km race time of 75 min or less, and could contribute to the ability of our runners to predict finishing times. Earlier studies have reported significant positive correlations between predicted and actual times for races ranging from 1 mile to 10 km [20], with our study extending findings to 12-km races.

##### 4.6. Plantar-flexion strength

Our study provides novel findings regarding plantar-flexion isometric strength post 12-km race in recreationally competitive runners, with a clear decline in performance (~10%). Unilateral heel raises performed to fatigue [13,14] are one of the most common clinical methods used to quantify plantar-flexor strength endurance. However, performing this test takes time and does not reflect bilateral plantar-flexion performance. In contrast, our bilateral isometric plantar-flexion test was able to detect fatigue in both plantar-flexors immediately post-race through a 10-s protocol. Alterations in plantar-flexor function might in part explain the declines in postural control observed, as previously shown that plantar-flexor fatigue alters postural control in healthy males, with values returning to baseline 20 min following muscular fatigue [36].

#### 4.7. Limitations

One limitation of this study is the relatively small sample size ( $n = 24$ ); however, post-hoc power analyses indicate sufficient power to detect differences with 80% power and 5% significance for COP<sub>path</sub>, COP<sub>area95</sub>, and left – right plantar pressure distribution. Due to time constraints, we elected to record one measure for most tasks following familiarisation, which does not account for intra-subject variability in performance. Given that any learning effect would likely have improved post-race performance, we may have shown a greater post-race change had participants undergone a more extensive familiarisation. Finally, since only one post-race testing session was undertaken (typically within 2 min of crossing the finish line), the persistence of the observed changes remains unknown.

#### 5. Conclusions

Running a 12-km race influenced neuromuscular measures linked with postural balance and plantar-flexion strength, confirming racing-induced fatigue in our recreationally competitive runners. Despite quantifiable declines in postural balance and plantar-flexion strength, self-selected foot-strike angle did not meaningfully change and might not be an appropriate indicator of fatigue, particularly in habitual rear-foot strikers. Our findings corroborate the importance of plantar-flexion strength in racing, and that postural control is altered in fatigued runners. Tracking postural control over time may be useful in the monitoring of training loads and recovery in runners. Finally, although our runners were able to predict their finishing times with a relatively high accuracy, their self-reported foot-strike patterns were not representative of their actual patterns in nearly 50% of cases. Objectively quantifying foot-strike patterns rather than using self-reported measures is recommended prior to making any inferences related to this gait characteristic.

#### Conflict of interest statement

None.

#### Authors' contributions

LM extracted data from the recorded videos, performed statistical analyses, and helped to draft the manuscript; CMB participated in the conception, design, and coordination of the study, and critically revised drafts of the manuscript; KHL participated in the conception, design, and coordination of the study, performed statistical analyses, helped to draft the manuscript, critically revised drafts of the manuscript, and lead the submission and revision process. All authors have read and approved the final version of the manuscript, and agree with the order of presentation of the authors.

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