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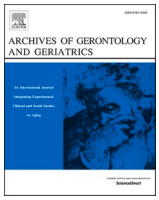

# Exploring new balance and gait factors that are associated with osteosarcopenia in patients with a previous fall and/or fracture history

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## HIGHLIGHTS

- Analysis of gait and balance in older adults with fall and/or fracture history.
- Those with osteosarcopenia performed poorly compared to osteopenia or osteoporosis.
- Balance parameters discriminate osteosarcopenia from osteopenia and osteoporosis.
- Decreased stability and grip strength combined are strong indicators of osteosarcopenia.

## ARTICLE INFO

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## ABSTRACT

Osteosarcopenic individuals have poor muscle function and increased bone fragility, which results in a severe detriment to health outcomes. Hence, there is a necessity to discover easily accessible factors associated with osteosarcopenia to develop timely interventions. This study aimed to determine new sensitive balance and/or gait variables that are associated with osteosarcopenia in a population of older people with a history of falls and/or fractures. In a cross-sectional cohort study, 306 men and women aged ≥65 years completed a series of questionnaires, clinical assessments and muscle strength and function tests. Subsequently, participants were separated into osteopenia, osteoporosis and osteosarcopenia, groups for comparison and further analysis. Osteosarcopenia performed worse than osteopenia and osteoporosis in grip strength, gait speed, physical function scores and in multiple gait and balance indices ($p<0.001$). During posturography testing, there were larger elliptical areas with eyes open ($p = 0.003$), and eyes closed ($p = 0.043$) and increased sway velocity on a firm platform ($p = 0.007$) in the osteosarcopenia group, compared to osteoporosis. Limits of stability and eyes open ellipse area significantly contributed to the multivariable model ($p = 0.029$ and $p = 0.038$, respectively), suggesting that these balance parameters, along with grip strength, may be useful in identifying older adults with osteosarcopenia from those with only osteopenia/osteoporosis. Older adults with osteosarcopenia and a history of falls and/or fractures demonstrated inferior strength, function, and gait characteristics. This study identified indices of balance that were sensitive discriminators for osteosarcopenia and could be easily implemented into routine assessment.

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## 1. Introduction

Osteosarcopenia is a relatively new term used to define the co-existence of osteopenia/osteoporosis and sarcopenia (Hirschfeld, Kinsella & Duque, 2017). The syndrome is common in older adults and is considered to affect mobility, increase the risk of falls and fractures, as well as be responsible for higher hospitalization rates (Kirk, Al Saedi & Duque, 2019; Nielsen et al., 2018). Whilst osteopenia (low bone mass; ≤−1.0 T-score), osteoporosis (low bone mass; ≤−2.5 T-score) and sarcopenia (low muscle mass, strength and function; described in detail shortly (Cruz-Jentoft et al., 2019)) negatively impact health outcomes in older adults, whether the negative association of osteosarcopenia on physical function is worse than either alone is unclear (B. Kirk, Zanker & Duque, 2020). Previous research does propose a link between bone and muscle loss (B. Kirk et al., 2020, 2020a), such that the risk factors for osteopenia, osteoporosis and sarcopenia, such as decreased hand grip strength (HGS), inability to ascend from a chair, slow gait speed, and balance problems, may be exacerbated in osteosarcopenia. Consequently, osteosarcopenic individuals are regarded as the most at risk population for fractures and further functional decline (B. Kirk et al., 2020), resulting in disability and mortality. As such, being able to identify those with osteosarcopenia has important clinical implications.

Falls are defined as the unexpected loss of balance, resulting in an individual coming to rest involuntarily on the ground, increasing the potential for bone fracture (Lamb et al., 2005; Huo et al., 2016). The current physical evaluations, such as HGS, short performance physical battery (SPPB), and timed up and go test (TUG), are effective in making a diagnosis and quantifying the severity of (osteo)sarcopenia (B. Kirk et al., 2020; Sepúlveda-Loyola et al., 2020). However, other variables are sensitive to falls and fractures, and therefore possibly to osteosarcopenia, that are not specifically measured in these tests. Current diagnoses of osteosarcopenia are low bone mass (≤−1.0 T-score)/-appendicular lean mass (≤7.0 kg/m$^2$ in men, ≤5.5 kg/m$^2$ in women), and decreased HGS (≤27 kg for men, ≤16 kg for women) (Cruz-Jentoft et al., 2019), although chair stand time can also be used (Zanker et al., 2023). These thresholds are based on the European working group definitions of sarcopenia, which were adopted in Australia and New Zealand (Zanker et al., 2019). Interestingly, despite balance problems being one of the leading causes of falling, balance indices are not included in current diagnoses.

The Balance Rehabilitation Unit (BRU), located at the Australian Institute for Musculoskeletal Sciences (AIMSS), uses newly reliable and validated methods that uses 3D virtual reality to assess postural control responses in 2D displacement, including limits of stability (LOS), center of pressure (COP), sway velocity and ellipse area, in response to various visual and vestibular scenes during four different conditions (Boersma et al., 2012). Low LOS (<170 cm$^2$) and high COP (>20 cm$^2$) are associated with high falls risk (Huo et al., 2016; Duque et al., 2013), and could therefore be possibly associated with osteosarcopenia.

Further, gait cadence and stride length are also variables sensitive to predicting falls and fractures. In a study by Matsumoto and colleagues, older adults diagnosed with knee osteoarthritis had large variations in step length, step width, and double leg support time. Consequently, their overall movement was inconsistent and increased their risk of falling (Matsumoto et al., 2015). In addition, Jacobs and colleagues analyzed gait parameters in individuals suffering from osteoporotic vertebral compression fractures. They tended to walk with shorter, faster and wider strides, and acquired an unstable body configuration, thus increasing their falls risk (Jacobs et al., 2020). While these results may be attributable to factors unrelated to osteosarcopenia, such as joint inflammation, there may be a relationship between balance and gait parameters and osteosarcopenia that could be associated with adverse outcomes, particularly in high-risk older population.

Despite the interrelationship between poor physical function and increased falls and fracture risk, prevention of falls and subsequent fracture fragility are under-prioritized and neglected by healthcare systems (Gielen et al., 2017). In addition, recent studies have mainly explored ways to improve bone mineral density (BMD), specifically in osteoporosis (Han et al., 2018), rather than exploring possible contributors. Likewise, recent sarcopenia research continues to argue about the specific definition of the condition (Han et al., 2018), as opposed to examining the reasons behind it. Therefore, there is a crucial necessity to inform researchers and clinicians about the significance of promptly identifying and managing osteosarcopenia (B. Kirk et al., 2020). Therefore, the primary objective of this cross-sectional study was to determine whether there are any new sensitive balance and/or gait variables that can identify and separate participants who have a history of falls/fractures with osteosarcopenia from those with osteopenia and osteoporosis alone, using a multivariable model.

## 2. Method

### 2.1. Participants

Participants aged ≥65 years that were referred to the Falls and Fracture Clinic (FFC) (Sunshine Hospital, Melbourne, Australia) and presented with any of the following history: multiple faller (≥2 in the last year), single faller with established balance and/or gait problem, unexplained fall with apparent complex medical cause(s), symptomatic or asymptomatic fragility fracture, and clinical or paraclinical BMD risk of fractures were included in the study. A total of 309 adult men and women were confirmed eligible and were requested to attend a screening session where they completed a series of questionnaires, underwent clinical assessments, including a whole-body dual-energy x-ray absorptiometry (DXA) scan, as well as performed different muscle strength and function assessments: hand grip strength (HGS), short physical performance battery (SPPB), timed up and go test (TUG), posturography and GAITRite, as described below. The current study was approved by the Western Health Office for Research (#QA2021.51) and was performed in accordance with the WMA Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects.

Only after all the above measurements had been completed, participants were separated into four groups: osteopenia (BMD ≤−1.0 T-score); osteoporosis (BMD ≤−2.5 T-score); sarcopenia (low appendicular lean mass [≤7.0 kg/m$^2$ in men, ≤5.5 kg/m$^2$ in women], and low HGS [≤27 kg for men, ≤16 kg for women]); and osteosarcopenia (BMD ≤−1.0 T-score, low HGS [≤27 kg for men, ≤16 kg for women] and low appendicular lean mass [≤7.0 kg/m$^2$ in men, ≤5.5 kg/m$^2$ in women]), for comparison and further analysis. With only 3 individuals classified in the sarcopenia group, suggests that muscle loss predisposes people to lose bone, particularly within this study cohort who have experienced problems associated with falls and fractures. Indeed, studies have shown those with sarcopenia are also most likely to also have osteopenia/osteoporosis (Yoshimura et al., 2017; Nielsen et al., 2020). As such, there were insufficient numbers for any meaningful analysis of the sarcopenia-only group, thus they were excluded from the final analysis. Consequently, statistical analysis was completed only on the 306 participants with osteopenia ($n$ = 64), osteoporosis ($n$ = 176) or osteosarcopenia ($n$ = 66).

### 2.2. Clinical assessments

Participants underwent numerous clinical assessments, including height (SECA stadiometer; nearest 0.1 meter), and weight assessments (TANITA electronic scales; nearest 0.1 kg), as well as a whole body DXA scan (Hologic Inc, Bedford, MA). DXA was carried out to evaluate both BMD and lean mass (for the diagnosis of osteopenia/osteoporosis and/or sarcopenia). In order to determine the associations between the clinical assessments as determined via DXA and physical performance, a series of functional measurements were conducted. By means of a Handheld Jamar Hydraulic Dynamometer (Sammons Preston Inc), the participants carried out three HGS trials in both hands. The sarcopenia and

osteosarcopenia cut off points for low grip strength were ≤27 kg for men and ≤16 kg for women (Dodds et al., 2014).

### 2.3. The short physical performance battery (SPPB)

A widely used falls-risk measurement tool is the SPPB whereby balance, gait speed and leg strength capabilities are evaluated (Guralnik et al., 1994). In this study, the SPPB was performed by all participants according to the general standards. Briefly, balance was assessed by accomplishing up to three hierarchical standing postures: the side-by-side stand, semi-tandem and tandem stand. Assessment of gait speed was performed in duplicate with the use of a GAITRite instrumented walkway system (CIRSystems Inc, Havertown, PA) where temporal and spatial parameters, in particular gait cadence, step length, stride length, single leg support, double leg support, and base of support were recorded. GAITRite is a pressure sensitive walkway that provides identification of gait abnormalities by recording and examining numerous gait cycles in a single walk (GAITRite: World Leader in Temporospatial Gait Analysis n.d.). The final task was the chair stand assessment, where participants were seated in a standard chair (47 cm high), with their arms folded across their chest and feet flat on the floor. Participants stood up once, while keeping their arms folded. If they were unable to stand without using their arms, the test was terminated, and the results were recorded. If the participant could complete the stand, they proceeded to five repeats.

Results were recorded and the scores from each test were combined to develop a total maximum SPPB score of 12, with each aspect scored from 0 (unable to complete the test) to 4 (highest level of performance) (Puthoff, 2008) (for specific scoring see supplementary Fig S1). The test indicated poor physical function and predicted osteosarcopenia when a score of less than 8 was acquired (Pavasini et al., 2016).

### 2.4. Timed up and go test (TUG)

A useful screening tool widely used by clinicians to evaluate a patient's risk of falling is the Timed Up and Go Test (TUG) (Schoene et al., 2013; Bretan et al., 2013). Integrated into the screening process of this study, participants executed two timed trials of the TUG according to the standard procedure (Podsiadlo & Richardson, 1991). Briefly, the time taken for the participant to rise from a chair, walk 3-meters as quickly and safely as possible, and then walking back to sit down on the same chair was recorded. Using the values obtained, the cut off TUG test scores for predicting osteosarcopenia were values greater than 10.85 s (Martinez et al., 2015).

### 2.5. The balance rehabilitation unit (BRU) assessment

To further evaluate indices of balance, postural control, and stability, the BRU assessment was performed as previously described (Phu et al., 2019). Briefly, for the BRU assessment, participants stood on a firm platform or foam block, shoes on, with feet positioned at shoulder width and arms resting along their body. LOS and postural control (which comprises COP, sway velocity and ellipse area) were measured during four different conditions involving various standing positions with eyes open or closed. The participants were requested to perform each condition for 60-seconds, without moving their feet or having assistance. If unable to do so at any point, the test was terminated. Postural measures was quantified via a posturography report automatically generated by the integrated software recording data directly from the pressure platform (Medicaa, Uruguay) (Huo et al., 2016; Gazzola et al., 2020).

### 2.6. Statistical analyses

Variables with normal distribution are expressed as mean ± SD, whereas abnormally distributed variables are presented as median with interquartile range (IQR). To determine if the data were normal, visual inspection of the frequency distribution (histogram) was used. Functional indicators, postural control indicators and gait indicators were compared between osteosarcopenia, osteopenia and osteoporosis group using one-way ANOVA or the Kruskal-Wallis test (Tukey test was used for post-hoc pairwise comparison), as appropriate, while a Chi-squared test was applied to sets of categorical data.

Furthermore, the relationship between parameters and osteosarcopenia was calculated using logistic regression analysis. To ensure confounding factors were not distorting any results, logistic regression was adjusted for age, body mass index (BMI) and sex. Area under the receiver operating characteristics curve (AUC) was calculated to assess the discriminative ability of each model to discriminate osteosarcopenia from osteopenia/osteoporosis. Variables with a p-value <0.2 in the logistic regressions were selected for the multivariable model (adjusted for age). To assess if any of those variables would improve classification of osteosarcopenia, a likelihood ratio test was performed to check the contribution of each variable to the model including hand grip strength and age. Statistical analyses were performed in JASP 0.14.1, GraphPad Prism 9 and SPSS Statistics 27, with an alpha value <0.05 indicating statistical significance.

## 3. Results

### 3.1. Participant characteristics

Demographic, anthropometric, health, and physical function characteristics of the participants were collected and presented in Table 1.

### 3.2. Osteosarcopenia is associated with a decrease across all assessments of physical function compared to osteopenic and osteoporotic patients

We found that the negative impact of osteosarcopenia on physical function was worse than osteopenia or osteoporosis alone. Pairwise comparisons showed lower HGS (Fig 1**A**), gait speed (Fig 1**B**), SPPB scores (Fig 1**C**), and longer TUG times (Fig 1**D**) in the osteosarcopenia group (all $p<0.001$) compared to both the osteopenia and osteoporosis groups. The osteoporotic group also performed worse than the osteopenic group in the HGS and TUG tests ($p = 0.002$ and $p = 0.037$, respectively; Fig 1**A and** 1**D**).

### 3.3. The osteosarcopenia group performed worse across indices of postural control

Osteoporosis and osteosarcopenia demonstrated significantly lower LOS than osteopenia ($p = 0.010$ and $p<0.001$, respectively**;** Fig 2**A**). There were significantly larger elliptical areas with eyes open on firm platform ($p = 0.003$**;** Fig 2**B**), and increased sway velocity with eyes open on firm platform ($p = 0.007$**;** Fig 2**C**) in the osteosarcopenic group compared to the osteoporotic group. Both osteopenia and osteosarcopenia were higher than osteoporosis for the eyes closed ellipse area variable ($p = 0.027$ and $p = 0.043$, respectively**;** Fig 2**D**). Lastly, there was no difference in the eyes closed sway velocity measurement between all groups (Fig 2**E**).

There were several participants that were not able to complete the balance task on the foam pillow with their eyes closed as part of the BRU. As a result, to see if any differences existed between the groups, the frequencies, and percentages of whether or not the participants could complete the test was calculated. More osteosarcopenic participants were unable to perform the foam eyes closed (FEC) task compared to those with osteopenia or osteoporosis (71.2% vs 28.1% and 35.2%, respectively, $p<0.001$).

### 3.4. Osteosarcopenia severely impairs gait compared to patients with osteopenia and osteoporosis

Differences in gait parameters between groups were analyzed using

**Table 1**
Characteristics of the participants.

| | All participants | Osteopenia | Osteoporosis | Osteosarcopenia |
|---|---|---|---|---|
| Number (%) | 306 (100) | 64 (20.9) | 176 (57.5) | 66 (21.6) |
| Age (years) | 77.4 ± 6.9 | 75.3 ± 6.8 | 77.25 ± 6.9 | 80.1 ± 6.4 |
| Sex (% women) | 76.1 | 62.5 | 81.2 | 75.8 |
| BMI (kg/m$^2$) | 28.31 (24.3, 31.4) | 30.7 (26.1, 34.0) | 27.6 (24.1, 30.3) | 27.8 (23.4, 30.7) |
| Number of falls | 2.3 (1.0, 3.0) | 2,1 (1.0, 3.0) | 2.1 (1.0, 3.0) | 3.1 (1.0, 3.3) |
| Number of fractures | 1.0 (1.0, 1.0) | 0.8 (0.0, 1.0) | 1.0 (1.0, 1.0) | 1.1 (1.0, 1.0) |
| BMD (T-score) | −3.0 ± 0.9 | −1.8 ± 0.4 | −3.4 ± 0.7 | −3.3 ± 0.9 |
| HGS (kg) | 21.0 (17, 29.0) | 29.0 (20.3, 34.0) | 22.0 ± (19.0, 28.8) | 13.5 ± (11.0, 15.0) |
| TUG (s) | 15.3 (11.1, 20.9) | 12.8 (9.8, 17.2) | 14.7 (10.5, 19.4) | 20.76 (16.0, 25.2) |
| SPPB total | 7.5 ± 2.4 | 8.13 ± 2.2 | 7.74 ± 2.5 | 6.29 ± 2.2 |
| Gait speed (m/s) | 0.8 ± 0.3 | 0.8 ± 0.3 | 0.8 ± 0.3 | 0.6 ± 0.2 |
| Gait cadence (steps/min) | 96.8 ± 17.6 | 101.1 ± 17.3 | 97.0 ± 17.5 | 91.7 ± 17.3 |
| Step length (cm) | 46.3 ± 11.6 | 49.2 ± 10.9 | 47.4 ± 11.5 | 40.0 ± 10.5 |
| Stride length (cm) | 93.1 ± 23.3 | 99.0 ± 21.9 | 95.4 ± 23.1 | 80.5 ± 21.1 |
| Single support (%GC) | 31.5 (28.4, 33.8) | 32.3 (30.2, 34.2) | 31.7 (29.6, 34.3) | 28.7 (25.8, 32.0) |
| Double support (%GC) | 37.9 (32.6, 43.9) | 36.1 (32.2, 40.5) | 37.4 (32.2, 41.1) | 43.2 (36.7, 48.2) |
| BOS (cm) | 10.2 (8.3, 13.2) | 11.5 (8.5, 14.2) | 10.2 (8.1, 12.8) | 10.2 (8.4, 13.2) |
| LOS (cm$^2$) | 119.9 ± 62.6 | 144.3 ± 63.3 | 118.1 ± 62.6 | 100.3 ± 53.6 |
| EOEA (cm$^2$) | 4.6 (2.5, 8.1) | 4.4 (2.6, 8.4) | 4.2 (2.3, 7.4) | 6.2 (3.4, 9.8) |
| EOS (cm/s) | 1.4 (1.0, 1.8) | 1.4 (1.0, 1.8) | 1.3 (1.0, 1.8) | 1.5 (1.2, 2.1) |
| ECEA (cm$^2$) | 5.2 (2.7, 9.2) | 6.3 (3.2, 10.9) | 4.6 (2.5, 8.3) | 5.6 (3.1, 9.9) |
| ECS (cm/s) | 1.9 (1.4, 2.6) | 2.2 (1.4, 2.8) | 1.9 (1.3, 2.6) | 1.9 (1.5, 2.8) |

Notes: Values are expressed as mean ± SD or median (IQR). Number of falls and Number of fractures are within the last year.
Abbreviations: BMI, body mass index; BMD, bone mineral density; HGS, hand-grip strength; TUG, timed up and go; SPPB, short physical performance battery; %GC,% gait cycle; BOS, base of support; LOS, limits of stability; EOEA, eyes open ellipse area; EOS, eyes open sway velocity; ECEA, eyes closed ellipse area; ECS, eyes closed sway velocity.

the GAITRite system and overall, it was found that the osteosarcopenia group performed worse compared to both osteopenia and osteoporosis groups (Fig 3**A-F**). As such, pairwise comparisons showed a lower gait cadence in osteopenic patients compared to those with osteosarcopenia ($p = 0.007$; Fig 3**A**). In addition to this, step length (Fig 3**B**), stride length (Fig 3**C**), and single leg support time (Fig 3**D**) were lower in the osteosarcopenia group (all $p<0.001$) compared to both the osteopenia and osteoporosis groups, indicative of a further decline in gait-related function. It was also identified that the osteosarcopenic group relied more on double leg support during their gait cycle ($p<0.001$; Fig 3**E**), thus potentially increasing their falls risk. In addition, there were no differences between all groups in base of support (Fig 3**F**).

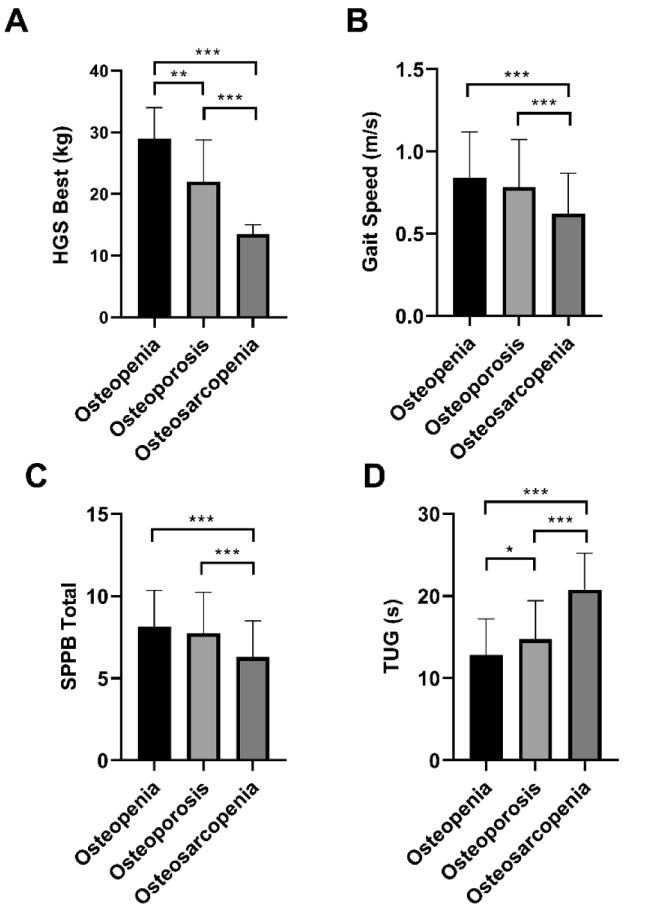


**Fig. 1.** Outcome measures from various physical evaluations. Maximum hand grip strength (HGS) measurement (A); gait speed (B); Short Physical Performance Battery (SPPB) score (C); timed-up and go test (TUG; D). Significance indicators: *$p<0.05$, **$p<0.01$, ***$p<0.001$ with values are plotted as mean ± SD or median (IQR).

### *3.4. Evaluation of various physical performance indicators as discriminators of osteosarcopenia*

A logistic regression was performed to ascertain the effects of current physical evaluations on the likelihood that participants have osteosarcopenia. As presented in Table 2, the odds of having osteosarcopenia is 40% lower (OR=0.61, 95% CI [0.53, 0.70]) if an individual has high HGS, 92% lower (OR=0.08, 95% CI 0.03, 0.26]) if an individual has fast gait speed, and 22% lower (OR=0.79, 95% CI [0.69, 0.89]) if an individual acquires high SPPB scores. There were 7% higher odds of having osteosarcopenia if an individual has longer TUG times (OR=1.07, 95% CI [1.03, 1.11]). The area under the curve (AUC) shows how well the logistic regression model correctly discriminates participants with an outcome vs without the outcome (AUC of 1.00 representing perfect discrimination). As displayed in Table 2, the AUC for HGS provides the best discrimination compared to the other physical evaluations, with similar values for gait speed, SPPB and TUG.

### *3.5. Evaluation of BRU parameters as discriminators of osteosarcopenia*

A logistic regression was performed to ascertain the effects of BRU parameters on the likelihood that participants have osteosarcopenia. As shown in Table 3, increasing LOS was associated with a decreased likelihood of osteosarcopenia, in which the parameter reduced the odds of osteosarcopenia by 1% (OR=0.99, 95% CI [0.99, 1.00]). There is 3% higher odds of having osteosarcopenia if an individual has high eyes open ellipse area (EOEA) scores (OR=1.03, 95% CI [1.00, 1.07]), and

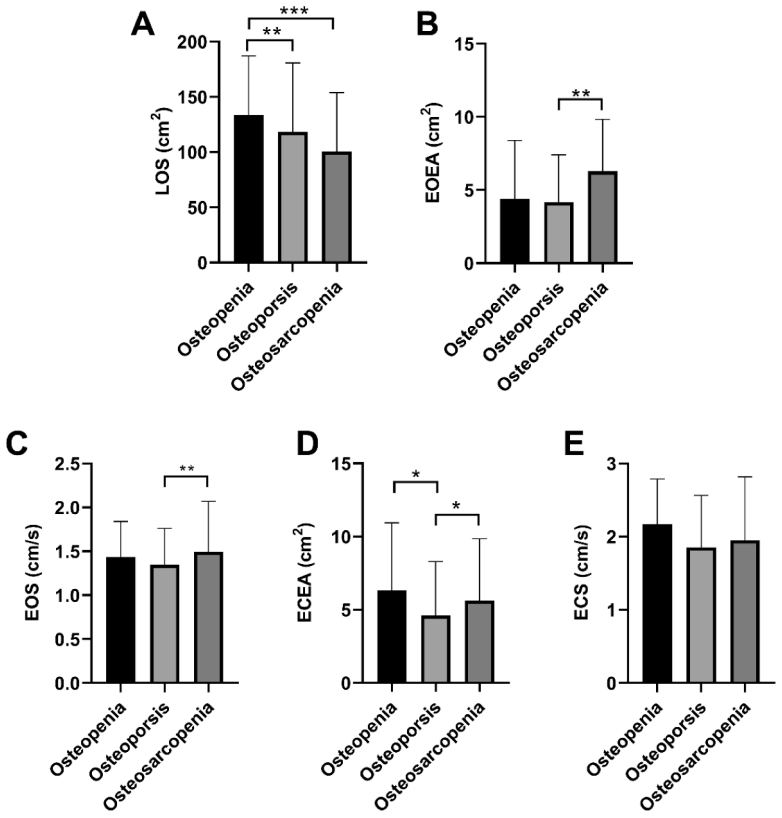


**Fig. 2.** Balance rehabilitation unit (BRU) measurements. Limits of stability (LOS; A); eyes open ellipse area (EOEA; B); eyes open sway velocity (EOS; C); eyes closed ellipse area (ECEA; D); eyes closed sway velocity (ECS; E). Significance indicators: $*p<0.05$, $**p<0.01$, $***p<0.001$ with values are plotted as mean ± SD or median (IQR).

46% higher odds ratio if an individual has high eyes open sway velocity (EOS) scores (OR=1.46, 95% CI [0.99, 2.15]). AUC values of the logistic regression models were similar in all variables (<0.7), indicating poor discrimination capabilities after adjusting for age, BMI and sex.

### *3.6. Evaluation of multiple GAITRite parameters as discriminators of osteosarcopenia*

A logistic regression was performed to ascertain the effects of GAITRite parameters on the likelihood that participants have osteosarcopenia. As displayed in Table 4, the odds of having osteosarcopenia is 2% lower (OR=0.98, 95% CI [0.97, 1.00]) if an individual has fast gait cadence, 6% lower (OR=0.94, 95% CI [0.91, 0.97]) if an individual has long step lengths, 3% lower (OR=0.97, 95% CI [0.96, 0.98]) if an individual has long stride lengths, and 14% lower (OR=0.86, 95% CI [0.80, 0.92]) if an individual has long single leg support times. In contrast, there were 7% higher odds of having osteosarcopenia if an individual has longer double leg support times (OR=1.07, 95% CI [1.04, 1.11]). Aside from gait cadence (0.67) and base of support (0.64), AUC values of the logistic regression models were similar in all variables (AUC=0.72/0.73) and indicated good discriminative capabilities after adjusting for age, sex and BMI.

### *3.7. LOS and EOEA are strong indicators of osteosarcopenia alongside HGS*

From the logistic regression analyses, the majority of parameters obtained a p-value <0.2; however, in a combined single logistic regression, only HGS, LOS, EOEA and gait cadence remained significant. HGS is included as it is an important indicator in the current diagnosis, therefore any new sensitive balance and gait variables were assessed in comparison to HGS. Table 5 shows that LOS and EOEA significantly contribute to the multivariable model ($p = 0.029$ and $p = 0.038$, respectively), suggesting that these balance parameters, together with HGS, have capabilities in identifying older adults with osteosarcopenia. To help determine if the variables indeed discriminate osteosarcopenia, the confounding factor age (the most influencing factor in the logistic regressions) was also adjusted for.

## 4. Discussion

In this study, we determined whether there were any new sensitive balance and/or gait variables that could discriminate osteosarcopenia from osteopenia and osteoporosis in older adults with a history of falls and/or fractures. Secondary to this, we estimated the prevalence of osteopenia, osteoporosis, sarcopenia and osteosarcopenia in a sample of older adults who attended the FFC, as well as measured the difference in physical function, balance, and gait between the conditions. Altogether, we found the negative impact of osteosarcopenia was worse on current physical function measures compared to osteopenia and osteoporosis alone. Those classified in the osteosarcopenia group also performed worse in the BRU and GAITRite assessments, and together with HGS the variables LOS and EOEA, which were found to be sensitive discriminators of osteosarcopenia.

After completing their DXA scan and physical evaluations, most participants were diagnosed with osteoporosis (57%). While this is very high for community-dwelling individuals, this was not surprising, given the initial recruitment was based on fracture(s), or referral from a GP due to a history of falls or functional concerns of older individuals. In a study involving people from the northwest region of Adelaide, South Australia, 1066 participants aged greater than 50 years were randomly selected to undergo DXA scanning. A broad range of socioeconomic areas were covered, and of the participants, 3.6% were diagnosed with osteoporosis (Gill et al., 2012). This confirms that in comparison with

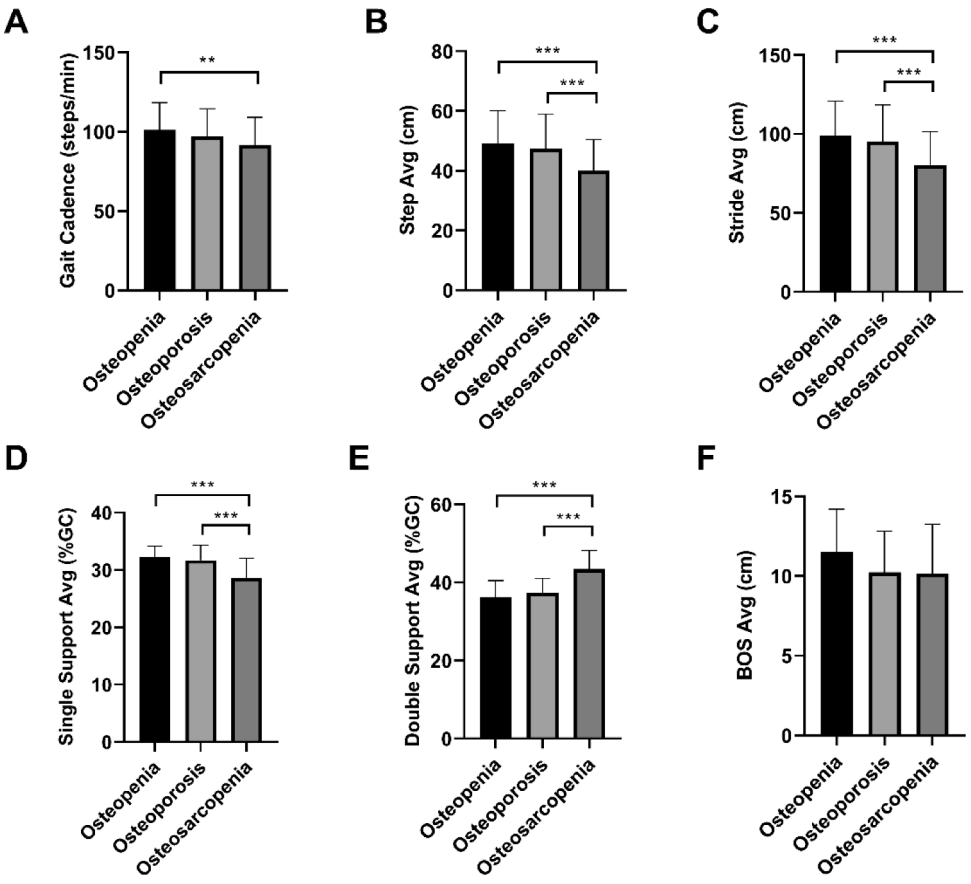


**Fig. 3.** Outcome measures of the GAITRite analysis. Gait cadence (A); step length average (B); stride length average (C); single leg support average (D); double leg support average (E) and average base of support (BOS; F). Significance indicators: $^{**}p<0.01$, $^{***}p<0.001$ with values are plotted as mean ± SD or median (IQR). Note - single and double leg support averages expressed as a percentage of gait cycle (GC).

**Table 2**
Likelihood predictors of osteosarcopenia as determined by logistic regression of current physical evaluations.

| | Odds Ratio (95% Confidence Interval) | p | AUC |
|---|---|---|---|
| HGS Best | 0.61 (0.53,0.70) | <0.001* | 0.93 |
| Gait Speed | 0.08 (0.03,0.26) | <0.001* | 0.69 |
| SPPB Total | 0.79 (0.69,0.89) | <0.001* | 0.71 |
| TUG | 1.07 (1.03.1.11) | <0.001* | 0.73 |

Notes: * $p<0.2$; Abbreviations: HGS, handgrip strength; SPPB, short physical performance battery; TUG, timed up and go.

**Table 3**
Likelihood predictors of osteosarcopenia as determined by logistic regression of various BRU parameters.

| | Odds Ratio (95% Confidence Interval) | p | AUC |
|---|---|---|---|
| LOS | 0.99 (0.99,1.00) | 0.018* | 0.67 |
| EOEA | 1.03 (1.00,1.07) | 0.064* | 0.65 |
| EOS | 1.46 (0.99,2.15) | 0.058* | 0.65 |
| ECEA | 1.01 (0.98,1.04) | 0.565 | 0.64 |
| ECS | 1.10 (0.89,1.37) | 0.377 | 0.64 |

Notes: * $p<0.2$; Abbreviations: LOS, limits of stability; EOEA, eyes open ellipse area; EOS, eyes open sway velocity; ECEA, eyes closed ellipse area; ECS, eyes closed sway velocity.

our sample, usual osteoporosis rates in the community are much lower. Furthermore, based on the 2017–2018 National Health Survey, 3.8% of the Australian population are estimated to have osteoporosis, with it being as high as 20% of people aged 75 years and older (Health, A.I.o. &

**Table 4**
Likelihood predictors of osteosarcopenia as determined by logistic regression of GAITRite parameters.

| | Odds Ratio (95% Confidence Interval) | p | AUC |
|---|---|---|---|
| Gait Cadence | 0.98 (0.97,1.00) | 0.031* | 0.67 |
| Step Length | 0.94 (0.91,0.97) | <0.001* | 0.72 |
| Stride Length | 0.97 (0.96,0.98) | <0.001* | 0.72 |
| Single Support | 0.86 (0.80,0.92) | <0.001* | 0.73 |
| Double Support | 1.07 (1.04,1.11) | <0.001* | 0.72 |
| BOS | 1.01 (0.94,1.09) | 0.767 | 0.64 |

Notes: * $p<0.2$.; Abbreviations: Avg, average; BOS, base of support.

**Table 5**
Likelihood ratio test – LOS, EOEA and gait cadence.

| Effect | Model Fitting Criteria | Likelihood Ratio Tests | | |
|---|---|---|---|---|
| | −2 Log Likelihood of Reduced Model | Chi-Square | df | p |
| **HGS Best** | 300.790 | 152.189 | 1 | <0.001*** |
| **LOS** | 153.390 | 4.789 | 1 | 0.029* |
| **HGS Best** | 302.449 | 153.376 | 1 | <0.001*** |
| **EOEA** | 153.390 | 4.316 | 1 | 0.038* |
| **HGS Best** | 300.520 | 147.302 | 1 | <0.001*** |
| **Gait Cadence** | 153.390 | 0.171 | 1 | 0.679 |

Notes: * $p<0.05$, *** $p<0.001$; Abbreviations: HGS, handgrip strength; LOS, limits of stability; EOEA, eyes open ellipse area Each model includes HGS, age and one of LOS/EOEA/Gait cadence.

Welfare 2020). Osteosarcopenia was the second largest group (21.4%), while only 3 individuals fell into the sarcopenia group (1%). In prior studies, it has been demonstrated that osteopenia/osteoporosis is frequent in sarcopenic individuals (Yoshimura et al., 2017; Nielsen et al., 2020), consistent with the low percentage of sarcopenia in the current study. This may be due to the fact that skeletal muscle contraction acts as a stimulus for BMD increases, indicating that low muscle mass and function would not be able to produce the strain required to uphold bone health or could be also due to alterations in the muscle/bone crosstalk (Girgis, Mokbel & Digirolamo, 2014). Hence, the prevalence of our groups reinforces the muscle-bone interrelation, in which the loss of muscle predisposes people also to lose bone, resulting in osteosarcopenia.

As exhibited in Fig 1, the participants in the osteoporosis group generally showed lower HGS, SPPB scores and gait speed, along with higher TUG times compared to the osteopenia group. Performance was expected to deteriorate from osteopenia to osteoporosis, since osteopenic individuals have bone density that is not as low and as detrimental (Karaguzel & Holick, 2010), although it is interesting that function, which is more muscle-related, appears to be associated with changes seen alongside bone, further supporting the idea of muscle-bone crosstalk. In the osteosarcopenia group, this decline in physical function was significantly worse, which indicates that combining the susceptibility of falling from sarcopenia with bone weakness in osteopenia/osteoporosis causes an adverse effect on physical function.

Given these functional deficits, it is not surprising that the physical evaluations are being used as an assessment of (osteo)sarcopenia. However, there are other variables sensitive to falls and fractures, and therefore possibly to the syndrome, that are not specifically measured in these tests. Indeed, we have observed BRU data indicative of poor balance (Phu et al., 2019; Rand et al., 2011), as well as differences in BRU parameters between osteosarcopenia, and osteopenia or osteoporosis alone. Both the osteoporosis and osteosarcopenia groups presented significantly lower LOS compared to the osteopenia group. LOS is correlated with static balance, with older adults often demonstrating reduced stability (Phu et al., 2019), signifying that osteosarcopenia induces further declines in balance. In addition, high ellipse area and high sway velocity are affiliated with poor balance, and thus an increased falls risk (Huo et al., 2016). The osteosarcopenia group had higher values than osteoporosis for the EOEA, EOS, and ECEA variables, further illustrating balance deficits. Similar to the current physical evaluations, performance was expected to deteriorate more in the osteosarcopenia group. Interestingly though, the osteopenic group also displayed higher ECEA scores compared to the osteoporotic group, indicating that the negative association of osteopenia on balance was worse than osteoporosis in this parameter. This is not in accordance with the literature, as mentioned earlier, osteopenia describes bone density that is not as low and supposedly detrimental as osteoporosis (Karaguzel & Holick, 2010). Thus, studies looking at the general mechanisms of action of the conditions may be required to explain these results. As a result of the higher ECEA in the osteopenia group, there was no significant difference compared to the osteosarcopenia group. This may be surprising at first glance; however, since the sample was of community-dwelling older adults with likely impairments in gait and/or balance, the eyes closed portion of the BRU was difficult for most. This is reinforced by the ECS velocity variable, as there were no significant differences between any of the groups. Further, many participants could not attempt the FEC task at all due to being even more challenging. Therefore, participants who could perform the FEC task were more functional given their condition. Indeed, more osteosarcopenic participants were unable to complete the FEC task (71.2%) compared to those with osteopenia or osteoporosis alone (28.1% and 35.2%, respectively). This corresponds to our findings from the other BRU variables, with the osteosarcopenic group demonstrating far less balance. This is not surprising given the results reported are only for those with decent balance to begin with, such that they could complete the eyes closed task. Moreover, the association between the groups and this ability to complete the test was significant. Hence, whether one can or cannot do the test could be a good screen for osteosarcopenia.

Similar to the BRU, we observed differences in GAITRite parameters between groups, with osteosarcopenia exhibiting worse gait than osteopenia or osteoporosis alone. Precisely determining abnormal gait in older adults is complicated; however, altered gait is often caused by underlying medical conditions (Thaler-Kall et al., 2015). A former study showed that frail participants compared to non-frail walked slower, with fewer steps per minute, and with shorter and wider steps. The same results were also found for participants with multimorbidity compared to those without, as well as for participants with a disability compared to those not disabled (Thaler-Kall et al., 2015). While abnormal gait is not readily defined, normative and population-based data can provide an understanding of what to expect in certain gait parameters (Hollman, McDade & Petersen, 2011). As such, we have observed GAITRite values outside of normative data (Hollman et al., 2011). Gait cadence, step length and stride length were lower in the osteosarcopenia group compared to both the osteopenia and osteoporosis groups. Older adults tend to have slow walking speeds, slow cadence and short stride lengths (Jerome et al., 2015), so the current results suggest that osteosarcopenia further declines gait function. This may be due to participants adapting to alterations in sensory or motor systems in an attempt to produce a more stable, and thus safer gait (Salzman, 2010). Alternatively, osteosarcopenia may contribute to the altered gait for reasons such as the syndrome causing muscle weakness, poor balance, fatigue, and muscle pain Salzman, (2010); The Voice of the Patient: Sarcopenia (n.d.). In addition, it was also identified that the osteosarcopenic group had shorter single leg support times and relied more on double leg support during their gait cycle. Double support refers to the%GC spent with both feet on the ground. It has been proposed that it relates to compensatory strategies to address balance impairments or fear of falling (Jerome et al., 2015). Osteosarcopenic participants in the present study presented with poor balance compared to osteopenia or osteoporosis alone. Therefore, this increased time in double leg support indicates that the participants adopted a more stable position in an attempt to compensate for their reduced stability. In actual fact though, longer double leg support times can cause inconsistencies in movement (Matsumoto et al., 2015); thus, osteosarcopenia are likely the most at risk group for falls.

Balance problems are one of the main causes of falling (Huo et al., 2016), and gait cadence and stride length are variables sensitive to predicting falls and fractures (Matsumoto et al., 2015; Jacobs et al., 2020). Despite this, not many studies have examined balance and spatiotemporal parameters in relation to osteosarcopenia. In our study, osteosarcopenic participants demonstrated significantly lower physical evaluations compared to both the osteopenia and osteoporosis groups. Logistic regressions ascertained that increasing LOS and gait cadence and decreasing EOEA are associated with a reduction in the probability of osteosarcopenia. Further, a likelihood ratio test showed that LOS and EOEA, together with HGS, have capabilities in identifying older adults with osteosarcopenia. Deteriorated performance in these parameters is associated with poor balance and high falls risk (Huo et al., 2016); therefore, they are currently being utilized for assessing and interpreting balance abnormalities in an aging population. However, considering we have identified an effect of LOS and EOEA on the probability that an individual aged greater than 65 years with fall & fracture history, and gait and balance issues has osteosarcopenia, the BRU parameter scores could be used to predict the prevalence and likelihood of developing the syndrome, although further research will be required to determine this. HGS was a stronger separator of osteosarcopenia compared to the balance parameters, as evident in the lower odds ratio, higher AUC value, and higher statistical significance, although this would be due to the use of HGS being part of the diagnosis of sarcopenia specifically. As such, because LOS and EOEA remained significant even against a very strong predictor, we propose that these balance indices could be as effective as HGS and could be included in current osteosarcopenia diagnoses.

However, all the parameters that showed some association on univariate analysis were then included in the multivariable model to evaluate which of these parameters showed the strongest association with osteosarcopenia. Using multiple outcome measures can increase the risk of false-positive findings. As a result, further validation of these results is needed before being applied in clinical practice.

This is the first study to examine physical function variables sensitive to osteopenia and osteoporosis, in order to discover potential discriminators for osteosarcopenia. An important strength of this study was the use of computerized posturography and gait analyzes, which provided a more valid, reliable, and objective determination of changes in balance and spatiotemporal parameters (Boersma et al., 2012; GAITRite: World Leader in Temporospatial Gait Analysis n.d.). In terms of the limitations of this project, it should be acknowledged that since only 3 individuals fell into the sarcopenia-only group, there was insufficient numbers for any meaningful analysis, but the prevalence suggests that loss of muscle may typically coincide with bone loss. As such, we were unable to examine the variables sensitive to sarcopenia, measure the negative association of sarcopenia on physical function, and subsequently compare the results to osteosarcopenia. Nor were we able to compare our results to non-fallers. Similarly, since these were participants with lower functional status to begin with, and limited to Victoria, whether the results are applicable to other populations of community-dwelling individuals requires further investigation. It is important to note that the results from this study, particularly pertaining to the gait and balance variables, can only be employed to those with a fall & fracture history, and/or gait & balance problems and those with osteosarcopenia. Also, the identified variables cannot discriminate osteosarcopenia patients from healthy individuals, only those who fall into osteoporosis or osteopenia categories. In summary, we found osteosarcopenic individuals had worse function as well as poorer balance and gait parameters than those with osteopenia or osteoporosis. We demonstrated that LOS and EOEA are indices that are associated with osteosarcopenia in older adults with a history of falls and fractures, along with gait and balance issues where non-completion of the BRU eyes closed task on the foam pillow also a possible sensitive discriminator. Thus, based on these data, we suggest that postural balance and comprehensive gait parameters could be integrated into definitions and/or screening processes of osteosarcopenia. These identified variables need to be tested to see if they can screen cases in the general population in future studies. Additionally, longitudinal and/or interventional studies should be performed to evaluate the predictive ability of the sensitive balance measures identified for osteosarcopenia.

## CRediT authorship contribution statement

**Danielle A Debruin:** Writing – review & editing, Writing – original draft, Visualization, Validation, Investigation, Formal analysis. **Kayley Miksa:** Writing – review & editing, Writing – original draft, Validation, Investigation, Formal analysis, Data curation. **Sara Vogrin:** Writing – review & editing, Software, Methodology, Formal analysis. **Gustavo Duque:** Writing – review & editing, Supervision, Project administration, Funding acquisition, Data curation. **Myrla Sales:** Writing – review & editing, Supervision, Project administration, Methodology, Investigation, Data curation, Conceptualization. **Alan Hayes:** Writing – review & editing, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Conceptualization.

## Declaration of Competing Interest

The authors have no conflicts of interest to declare in relation to the work performed in the manuscript entitled “Exploring new balance and gait factors that are associated with osteosarcopenia”.

## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.archger.2023.105221.

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