Successful 10-second one-legged stance performance predicts survival in middle-aged and older individuals

Claudio Gil Araujo, Christina Grüne de Souza e Silva, Jari Antero Laukkanen, Maria Fitariane Singh, Setor Kunutsor, Jonathan Myers, Joao Felipe Franca, Claudia Lucia Castro

ABSTRACT

Objectives Balance quickly diminishes after the mid-50s increasing the risk for falls and other adverse health outcomes. Our aim was to assess whether the ability to complete a 10-s one-legged stance (10-second OLS) is associated with all-cause mortality and whether it adds relevant prognostic information beyond ordinary demographic, anthropometric and clinical data.

Methods Anthropometric, clinical and vital status and 10-s OLS data were assessed in 1702 individuals (68% men) aged 51–75 years between 2008 and 2020. Log-rank and Cox modelling were used to compare survival curves and risk of death according to ability (YES) or inability (NO) to complete the 10-s OLS test.

Results Overall, 20.4% of the individuals were classified as NO. During a median follow-up of 7 years, 7.2% died, with 4.6% (YES) and 17.5% (NO) on the 10-s OLS. Survival curves were worse for NO 10-s OLS (log-rank test=85.6; p<0.001). In an adjusted model incorporating age, sex, body mass index and comorbidities, the HR of all-cause mortality was higher (1.84 (95% CI: 1.23 to 2.78) (p<0.001)) for NO individuals. Adding 10-s OLS to a model containing established risk factors was associated with significantly improved mortality risk prediction as measured by differences in −2 log likelihood and integrated discrimination improvement.

Conclusions Within the limitations of uncontrolled variables such as recent history of falls and physical activity, the ability to successfully complete the 10-s OLS is independently associated with all-cause mortality and adds relevant prognostic information beyond age, sex and several other anthropometric and clinical variables. There is potential benefit to including the 10-s OLS as part of routine physical examination in middle-aged and older adults.

INTRODUCTION

Aging is associated with a progressive decline in physical fitness and reductions or impairments in components of aerobic and non-aerobic fitness, including muscle strength/power, flexibility, balance and body composition. It is also well-established that the combination of sarcopenic obesity and loss of flexibility and balance are detrimental for overall health, placing older adults with frailty more prone to falls and other serious adverse medical sequelae. Indeed, falls are the second leading cause of unintentional injury-based deaths worldwide. Unlike aerobic fitness, muscle strength and flexibility, balance tends to be reasonably preserved until the sixth decade of life, when comparatively, it starts to diminish quickly.

Nevertheless, balance assessment is not routinely incorporated in the clinical examination of middle-aged and older individuals. This may be partly attributable to the poor standardisation of balance testing as well as to the relative paucity of data-relating balance results to clinical outcomes other than falls, such as mortality, when compared with, for example, aerobic fitness.

In this context, the availability of simple, inexpensive, reliable and safe balance assessment tools that could help predict survival would potentially be beneficial to health professionals evaluating and treating older adults. Therefore, the aims of our study were: (1) to assess whether the ability to complete a 10-s one-legged stance (10-s OLS) test was independently associated with all-cause mortality in middle-aged and older men and women and (2) whether the 10-s OLS added relevant prognostic information beyond ordinary demographic, anthropometric and clinical data. If the ability to perform this simple physical task were shown to be a good prognostic indicator for risk of all-cause mortality, it might be a useful complement to routine evaluations among middle-aged and older subjects.

METHODS

This was a prospective cohort study using data from the CLINIMEX Exercise open cohort/evaluation protocol (see online supplemental materials). Briefly, the CLINIMEX Exercise cohort study was set up in 1994 to assess the relationships of various measures of physical fitness and other exercise-related variables, as well as conventional cardiovascular risk factors with all-cause and cause-specific mortality outcomes. The sample size of 1593 participants was calculated based on the following parameter specifications: (1) level of significance, two-sided test at α=0.05; (2) power (1−β) of 80%; (3) 7% of the study participants dying during follow-up; (4) an SD of 0.5 for the exposure (given that the binary exposure follows a Bernoulli distribution with the probability of a subject achieving success, p, assumed to be equal to 0.5, the SD was calculated from the formula: (p*(1−p))1/2 and (5) effect size: the minimum HR considered to be clinically important, in this case, 1.7. The current analysis included 1702 participants aged 51–75 years at their first evaluation conducted between 10 February 2009 and 10 December 2020, who voluntarily sought the clinic for evaluation to assess...
aerobic and non-aerobic physical fitness and/or to obtain exercise counselling.

Censoring of vital status and mortality was updated to mid-December 2020 from the regional official registry data. All participants read and signed an informed consent and formally authorised the use of their deidentified data for scientific purposes. The study protocol was included in a National Research Registry and formally reviewed and approved by an external Research Ethics Committee (Plataforma Brasil—CAAE: 40122320.8.0000.9433). Cohort data are maintained in an institutional database.

Demographics, anthropometric and clinical variables
Sex, age, date of evaluation, date of death (if it occurred), censored date and follow-up time were available for all participants. Anthropometric measurements were obtained with participants barefoot and using minimal clothing and included height, weight, sum of six skinfolds—tricipital, subscapular, suprailiac, abdominal, thigh and medial calf - and waist girth measured at the umbilical level, as well as two calculated values—body mass index (BMI) and waist-height ratio. Clinical data were obtained by medical history, considering the presence or absence of known relevant diseases and/or use of regular medications. Obesity was defined as a BMI ≥30 kg/m². Less than 1% of anthropometric or clinical data were missing. All participants were fully ambulatory and those presenting with unstable gait or having signs of any known acute vestibular or otoneurological disturbance were excluded.

One-legged stance balance assessment
As part of the evaluation, participants were asked to stand on a flat platform. Static balance was assessed as the ability to complete 10 s in OLS, either left or right foot, under close face-to-face supervision of a physician and/or a nurse assistant as a precaution to prevent falls or injuries. To minimise the influence of muscle strength and flexibility and to improve standardisation, barefoot participants were instructed to place the dorsal part of the non-support foot on the back of the opposite lower leg, as naturally as possible (figure 1). Additionally, participants were asked to keep their elbows extended, the arms naturally placed close to their body and instructed to fix their gaze on an eye-level point at a 2-m distance. Once the participant assumed the correct position, a count of 10 s was started and up to three attempts were allowed. A very simple criterion was applied—ability to complete 10-s OLS on either foot, keeping the correct initial position and without any other support—and participants were accordingly classified as ability (YES) or inability (NO) to complete the 10-s OLS test.

Statistical analysis
For descriptive statistics, quantitative variables were described using mean±SD or median and IQR, depending on the nature of distribution, and categorical variables were summarised using frequencies and percentages. Sample size calculations employed the Stata command “stpower cox” which implements the methods of Hsieh and Lavori and Schoenfeld. The Cochran–Armitage test was used to test for temporal trends in deaths across the follow-up period. Results for YES and NO 10-s OLS were compared by two-tailed Student’s t-tests or χ² test, after checking, respectively, for the normality of distribution and homogeneity of variance and for the inexistence of expected cell count less than 1 and no more than 20% of cell counts less than 5, depending on the variable. Spearman rank correlation coefficients were used to calculate associations. Kaplan-Meier curves were constructed and log-rank tests were used to analyse survival times for the YES and NO 10-s OLS groups.

While the CLINIMEX Exercise cohort comprises men and women from 6 to 99 years of age, only participants aged between 51 and 75 years were included in this mortality study, as survival curves (see online supplemental materials) calculated at each 5 years of age interval starting at 41–45 years indicated that the combination of relevant numbers of deaths and failures to complete the 10-s OLS test could be identified only using the 51–75 years of age range. The relationship between 10-s OLS results and all-cause mortality was modelled by Cox univariate and multivariable analyses, after confirmation of no departure from the proportionality of hazards assumptions using Schoenfeld residuals. The proportionality test of each covariate as well as a global test was done. The test was not statistically significant for each of the covariates, and the global test was
also not statistically significant. Adjustments were made for age, sex, BMI and clinical variables (as previously described), using the 10-s OLS YES group as the reference. For each participant, follow-up time was obtained using the number of days between the evaluation and death or censoring dates. None of the participants were lost to follow-up.

To assess whether adding information on 10-s OLS to conventional risk factors was associated with improvement in the prediction of all-cause mortality, three statistical approaches were employed. First, the improvement in risk discrimination resulting from adding information on 10-s OLS to a model containing established risk factors (age, sex, BMI, medical history of coronary artery disease, hypertension, diabetes and dyslipidaemia) was quantified using Harrell’s C-index. Comparison of the C-index for models including and not including information on the 10-s OLS was performed according to the methodology of DeLong. The 95% CIs for C-indices and their changes were derived from jackknife SE. The C-index is appropriate for time-to-event data and provides the probability that the model correctly predicts the order of failure of randomly selected pairs of individuals. A C-index of 1.0 indicates perfect prediction of the order of failure (in this case, mortality), whereas a C-index of 0.5 is achieved purely by chance. Second, the continuous net reclassification improvement (NRI) was calculated, which determines whether risk increases cases applying a new model compared with an established or reference model. Additionally, the integrated discrimination improvement (IDI) was calculated, which integrates the NRI over all possible cut-offs. In addition to Harrel’s C-index which can be insensitive in detecting differences because it is based on ranks rather than on continuous data and not being able to assess calibration, we tested for differences in the −2 log likelihood of prediction models with and without inclusion of 10-s OLS. The −2 log likelihood test has been recommended as a more sensitive risk discrimination method. Statistical significance level was set at 5%, and 95% CIs were calculated for all results. Calculations were performed and figures prepared using either Prism (V.8.4.3; GraphPad, USA) or STATA (V.16; USA) statistical packages.

**Results**

The mean±SD age of the participants was 61.7±6.8 years and 68% were men. No adverse medical events or accidents occurred during the 10-s OLS testing. A total of 348 (20.4%) participants failed to pass the test and were classified as NO. The inability to complete the test, that is, 10-s OLS with either the right or left foot, increasing with aging, practically doubling at each subsequent 5-year age-group intervals beginning at age group of 51–55 years. The proportion of NO responders was 4.7% among those 51–55 years, 8.1% at 56–60 years, 17.8% at 61–65 years and 36.8% at 66–70 years. In the age group of 71–75 years, the majority of the participants (53.6%) were unable to successfully complete the 10-s OLS (figure 2). During a median (IQR) follow-up time of 7 (4.16–9.41) years, 123 participants (7.2%) died, mostly due to cancer (32%), cardiovascular causes (30%), diseases of the respiratory system (9%) and COVID-19 complications (7%) with no clear temporal trends in the deaths (p=0.77). Given a sample of 1702 individuals including 123 all-cause mortality events, we had 92% power to detect a clinically important HR of 1.84. The proportion of deaths in the NO group was higher than that in the YES group (17.5% vs 4.6%; p<0.001), reflecting an absolute difference of 12.9%, but the distribution of the major underlying causes of death did not differ significantly between the YES and NO groups (p=0.45).

A comparison of key variables for all participants and separately for 10-s OLS YES and NO groups is presented in table 1. While sex distribution did not differ significantly between the YES and NO groups, (p=0.76), several other variables including age, BMI and waist-height ratio differed between the two groups (p<0.001). In general, NO participants had an unhealthier profile with a higher percentage of participants having coronary artery disease, hypertension, dyslipidaemia and obesity. The most striking difference was for diabetes mellitus, which was three times more common in the NO group (37.9%) as compared with the YES group (12.6%) (p<0.001).

Correlation coefficients between a NO 10-s OLS response and age and several anthropometric variables of potential interest are shown in figure 3. With the exception of height, inability to complete the 10-s OLS was significantly associated with all the other variables (p<0.001). The two highest correlation coefficients between NO and selected continuous variables were 0.40 for age and 0.26 for waist-height ratio.

**10-s OLS and all-cause mortality association and risk prediction**

Kaplan-Meier survival curves were significantly different for YES and NO responders (p<0.001) (figure 4). Cox proportional hazard analysis indicated that inability to complete the 10-s OLS was associated with a significantly higher risk for all-cause mortality. An age-adjusted and a multivariable-adjusted—age, sex, BMI and clinical comorbidities (including history of coronary artery disease, hypertension, diabetes, obesity and dyslipidaemia) showed HRs (95% CI) of 2.18 (1.48 to 3.22; p<0.001) and 1.84 (1.23 to 2.78; p=0.003), respectively (table 2). A directed acyclic graph showing a minimally sufficient set of confounders for adjustment is also presented (figure 5).
An all-cause mortality model containing established risk factors yielded a C-index of 0.7990 (0.7563, 0.8417). After addition of the 10-s OLS binary results, the C-index was 0.8090 (0.7678, 0.8503), an increase of 0.0100 (–0.0005, 0.0205; p=0.06). The −2 log likelihood model showed significant improvement after addition of the 10-s OLS binary results to the model (p for comparison=0.002). The continuous NRI and IDI were 17.50% (95% CI −1.46 to 36.45; p=0.07) and 0.0143 (95% CI 0.0019 to 0.0267; p=0.024), respectively, suggesting additive value of the inability to complete the 10-s OLS test.

DISCUSSION

Each year an estimated 684 000 individuals die from falls globally, of which over 80% are in low/middle-income countries. There is considerable evidence that loss of balance is also detrimental for health and that some exercise interventions may improve balance. However, it

Table 1 Demographic and clinical characteristics of men and women aged 51–75 years according to the ability to complete 10-s one-legged stance test

<table>
<thead>
<tr>
<th>Variable*</th>
<th>Total (N=1702)</th>
<th>10-s one-leg stance test</th>
<th>P value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>61.7±6.8</td>
<td>60.3±6.2</td>
<td>67.2±6.0</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>67.9</td>
<td>68.1</td>
<td>67.2</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>79.9±16.0</td>
<td>79.0±15.5</td>
<td>83.6±17.3</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>169.9±9.2</td>
<td>171.1±9.1</td>
<td>169.1±8.6</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>27.6±4.5</td>
<td>27.2±4.2</td>
<td>29.2±5.2</td>
</tr>
<tr>
<td>Waist-height ratio</td>
<td>0.57±0.07</td>
<td>0.56±0.07</td>
<td>0.61±0.08</td>
</tr>
<tr>
<td>Sum of skinfolds (mm)‡</td>
<td>117.7±1.0</td>
<td>114.6±1.1</td>
<td>129.7±2.4</td>
</tr>
</tbody>
</table>

Comorbidities

| Hypertension (%) | 47.9 | 43.5 | 65.3 | <0.001 |
| Dyslipidaemia (%) | 54.8 | 52.7 | 63.0 | 0.001 |
| Diabetes mellitus (%) | 17.7 | 12.6 | 37.9 | <0.001 |
| Obesity (%) | 26.2 | 22.6 | 40.2 | <0.001 |
| Coronary artery disease (%) | 32.1 | 30.0 | 40.5 | <0.001 |
| Myocardial infarction (%) | 16.1 | 15.4 | 18.8 | 0.124 |
| CABG (%) | 8.7 | 7.5 | 13.3 | 0.001 |
| PCI (%) | 21.7 | 20.7 | 25.4 | 0.057 |
| Death (%) | 7.2 | 4.6 | 17.5 | <0.001 |
| Follow-up time (days) | 2538 (1518–3434) | 2628 (1594–3491) | 2123 (1146–3156) | <0.001 |

*Mean±SD or %.
†Student’s t-test or \( \chi^2 \) test.
‡Sum of six skinfolds—tricipital, subscapular, suprailiac, abdominal, anterior thigh and medial calf.
CABG, coronary artery bypass graft; PCI, percutaneous coronary intervention.

Figure 3 Spearman correlation coefficients between the inability to complete the 10-s one-legged stance test and demographic and anthropometric variables. Values of \( r > 0.048 \) (positive or negative) were significant at 5% of probability.

Figure 4 Kaplan-Meier survival curves of participants aged 51–75 years old divided by ability (YES) and inability (NO) to complete the 10-s one-legged stance test.
is currently uncertain if the results of repeated 10-s OLS tests would be amenable to intervention, that is, exercise or balance training, and if changes in 10-s OLS over time would influence mortality risk.\footnote{38}

In our 13 years of clinical experience routinely using the 10-s OLS static balance test in adults with a wide age range and diverse clinical conditions,\footnote{39} the test has been remarkably safe, well-received by the participants, and importantly, simple to incorporate in our routine practice as it requires less than 1 or 2 min to be applied.

### Table 2  
Associations of ability to complete 10-s one-legged stance balance test (10-s OLS) with all-cause mortality in 1702 men and women aged 51–75 years old (123 deaths, 7.2%; median follow-up time=7 years)

<table>
<thead>
<tr>
<th>10-s OLS</th>
<th>Events/ participants</th>
<th>All-cause mortality hazard ratio (HR)</th>
<th>(P) value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1—unadjusted</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>YES</td>
<td>62/1354</td>
<td>1 (Reference)</td>
<td></td>
</tr>
<tr>
<td>NO</td>
<td>61/348</td>
<td>4.58 (3.21 to 6.53)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Model 2—adjusted by age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>YES</td>
<td>62/1354</td>
<td>1 (Reference)</td>
<td></td>
</tr>
<tr>
<td>NO</td>
<td>61/348</td>
<td>2.18 (1.48 to 3.22)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Model 3—adjusted by age, sex, BMI and comorbidities†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>YES</td>
<td>62/1354</td>
<td>1 (Reference)</td>
<td></td>
</tr>
<tr>
<td>NO</td>
<td>61/348</td>
<td>1.84 (1.22 to 2.77)</td>
<td>0.003</td>
</tr>
</tbody>
</table>

* Cox proportional hazards modelling.  
† Model 3: adjusted by age, sex, BMI and presence of coronary artery disease, systemic arterial hypertension, dyslipidaemia and diabetes mellitus.

BMI, body mass index.

### Prognostic information

The ability to complete the 10-s OLS test starts to progressively diminish with ageing, approximately halving at each subsequent 5-year age group interval. Stated differently, the participants in the oldest age group—71–75 years—were more than 11 times more likely to be a NO responder as compared with those just 20 years younger and belonging to the youngest age group in the study—51–55 years. The ability to complete the 10-s OLS tended to show both a ceiling and a floor in terms of an age profile, with very rare (<1%) younger participants (<45 years of age) failing and relatively few participants older than 80 years able to complete the test (see online supplemental material).

Univariate analysis indicated that a NO 10-s OLS response was significantly and directly associated with age, with a high waist-height ratio and the prevalence of diabetes mellitus. Our results are concordant with those of Neri et al\cite{40} who found that adiposity measures, in particular waist circumference, were associated with postural instability and higher risk of falls in older adults. In addition, the higher percentage of participants with diabetes mellitus in the NO 10-s OLS group suggests that some of these participants have subclinical central or autonomic nervous system dysfunction, as has been recently reported.\footnote{41}

Our data show that middle-aged and older participants unable to complete the 10-s OLS had lower survival over a median of 7 years compared with those able to complete the test, with an 84% higher risk of all-cause mortality, even when other potentially confounding variables such as age, sex, BMI and clinical comorbidities or risk factors, including presence of coronary artery disease, hypertension, obesity, dyslipidaemia and diabetes mellitus, were taken into account. The utility of the 10-s OLS test for mortality risk assessment is further corroborated by the fact that it provided an improvement in mortality risk discrimination using measures including IDI and difference in \(-2\) log likelihood.

### Comparison of current findings with the literature

A study published in 2007\footnote{15} proposed normative values for OLS timing based on results obtained in 549 men/women divided into six age groups ranging from 18 to 80+ years. Similar to our study, they found that OLS performance was strongly and negatively influenced by age but unaffected by sex.\footnote{15} There is limited information in the literature relating balance to all-cause mortality. In a recent Japanese study with 1085 elderly participants (65–89 years),\footnote{22} it was observed that OLS timing was strongly associated with all-cause mortality, with an adjusted-relative risk value similar to the current study using similar covariates (1.91 (95% CI 1.39 to 2.63)). In a recent cohort study, Cao et al\footnote{42} evaluated static balance in 5816 men and women older than 40 years who were followed for a median of 12.5 years and observed that those with a balance disorder had a 44% higher risk of all-cause mortality when compared with those having normal results in the four conditions assessed in the modified Romberg test of standing balance on firm and compliant support surfaces.

It should be pointed out that OLS has been used to assess balance for more than 50 years; Fregly et al\footnote{43} were the first to report normative standards for OLS based on a healthy sample of military men and women. It is notable that in most studies OLS results were expressed as time in seconds, often limited to 30 or 60 s, reflecting the duration that participants were able to maintain the OLS position.\footnote{15} It is possible for young adults, it becomes progressively more difficult with ageing. Indeed, our data indicate that most of participants aged >70 years were unable to complete 10-s OLS. Moreover,
while it seems that reliability is moderate to good for timing OLS studies, it is possible that in a clinical setting with older participants timing measurements tend to be less reproducible due to high intraparticipant and interobserver variation, potentially limiting the validity of the OLS results. Additionally, there are distinct ways in which OLS has been assessed, with variations in arm/hand positions, whether arm movements for stabilisation are allowed and position of the opposite leg and foot, with some of the studies allowing a swing leg that incorporates a muscle strength component.

Therefore, our results are not only confirmatory of the studies mentioned above, but they extend these observations and make them practical for routine clinical use. Indeed, it is simpler and likely more reproducible to have a clear time reference such as 10 s as used in the current study, as compared with recording the time in which the subject is able to remain in OLS.

Strengths

There are several strengths to our study. The 10-s OLS testing was carried out in well-controlled situations and under direct health professional surveillance. The 10-s OLS test was easy to explain to the participant, to apply and to obtain the binary result used in the study (YES or NO responder). Median follow-up time and the percentage of deaths in the sample provided appropriate statistical power for analysis and to address the aim of the study. In addition, there were data available from several anthropometric and clinical variables that were used for clinically relevant multivariable modelling.

Limitations

Some limitations are notable. First, this CLINIMEX Exercise cohort is primarily composed of participants of white race and belonging to higher socioeconomic strata in Brazil. Any extrapolation of these findings to populations distinct from this profile should be interpreted with caution. It is also possible that a more sophisticated measure of OLS balance, such as centre of pressure displacement in a given period of time, would provide better discrimination and improve the value of this assessment in terms of survival. However, this would make testing much more difficult to incorporate as a simple clinical routine practice. Second, use of HRs may be uninformative because they make direct comparisons between risk factors difficult to interpret. They also imply a constant relative hazard throughout the follow-up, which is usually not the case. In addition, they have a built-in selection as a result of conditioning on those who have survived. Third, several potential confounder variables were not available for the participants, including recent history of falls, pattern of physical activity or exercise and sports practice, diet, smoking and the use of medications that may interfere with balance. Fourth, since we did not have repeat measurements of the exposure, we were unable to address time-varying confounding as well as time-varying confounding affected by prior exposure as potential confounders and to provide us the chance to correct for potential regression dilution bias and, finally, we have not used the K-fold cross-validation’s approach, due to the relatively limited sample size of our study. Future studies should explore whether 10-s OLS results add prognostic information when data are available for other components of physical fitness.

Finally, investigation of the biological mechanisms that may explain the observed associations between poor OLS balance and all-cause mortality is required. It is also of interest to investigate whether more detailed or sophisticated assessments of static balance, such as including a measurement of the centre of pressure displacement, number of trials required, different arm or foot positions and/or using closed eyes during the OLS, could contribute to even more powerful survival analyses.

CONCLUSION

Our study indicates that the inability to complete a 10-s OLS in middle-aged and older participants is related to a higher risk of all-cause mortality and, consequently, to a shorter life expectancy.

Twitter Claudio Gil Araujo @cgsaraujo

Acknowledgements The authors thank all participants who voluntarily permitted us to anonymously use their data and to the Secretary of Health of Rio de Janeiro state for providing the vital data information to the participants of CLINIMEX Exercise cohort.

Contributors CGA, CGSS, CLC and JFF were involved in the planning of the study and collecting data. Statistical analysis: CGA, CGSS, SK, JAL. Interpreting data: CGA, CGSS, MF, IM, SK, JAL. Manuscript writing and revising: all authors. CGA acts as the guarantor of the study.

Funding CGA was partially sponsored by research grants from national and local governmental agencies. Partial financial support was provided by CNPq e FAPERJ research agencies.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, conduct, reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Ethics approval This study involves human participants and was approved by the Ethics Committee COENP Brazilian Government (reference no: 4,459,555). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request. Deidentified data are available on reasonable request.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

ORCID iDs
Claudio Gil Araujo http://orcid.org/0000-0001-6679-6695
Christina Grüné de Souza e Silva http://orcid.org/0000-0002-0758-5174
Jari Antero Laukkanen http://orcid.org/0000-0002-3738-1586
Maria Fiatarone Singh http://orcid.org/0000-0002-1897-8707
Setor Kunztor http://orcid.org/0000-0002-2625-0273
Jonathan Myers http://orcid.org/0000-0003-2592-136X
João Felipe Franca http://orcid.org/0000-0001-6681-4152
Claudia Lucia Castro http://orcid.org/0000-0002-6833-0407