

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

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## 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

Ageing is associated with a progressive decline in physical fitness<sup>1–3</sup> and reductions or impairments in components of aerobic<sup>4 5</sup> and non-aerobic fitness, including muscle strength/power, flexibility, balance and body composition.<sup>6–11</sup> 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.<sup>12</sup> Indeed, falls are the second leading cause of unintentional injury-based deaths worldwide.<sup>13</sup> Unlike aerobic fitness,<sup>2 14</sup> muscle strength<sup>9</sup> and flexibility,<sup>8</sup>

balance tends to be reasonably preserved until the sixth decade of life, when comparatively, it starts to diminish quickly.<sup>15 16</sup>

Nevertheless, balance assessment is not routinely incorporated in the clinical examination of middle-aged and older individuals.<sup>17</sup> 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.<sup>16 18 19</sup>

In this context, the availability of simple, inexpensive, reliable and safe balance assessment tools<sup>11</sup> 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).<sup>11 20 21</sup> 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  $\alpha=0.05$ ; (2) power  $(1-\beta)$  of 80%; (3) 7% of 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:  $(p*(1-p))^{0.5}$  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

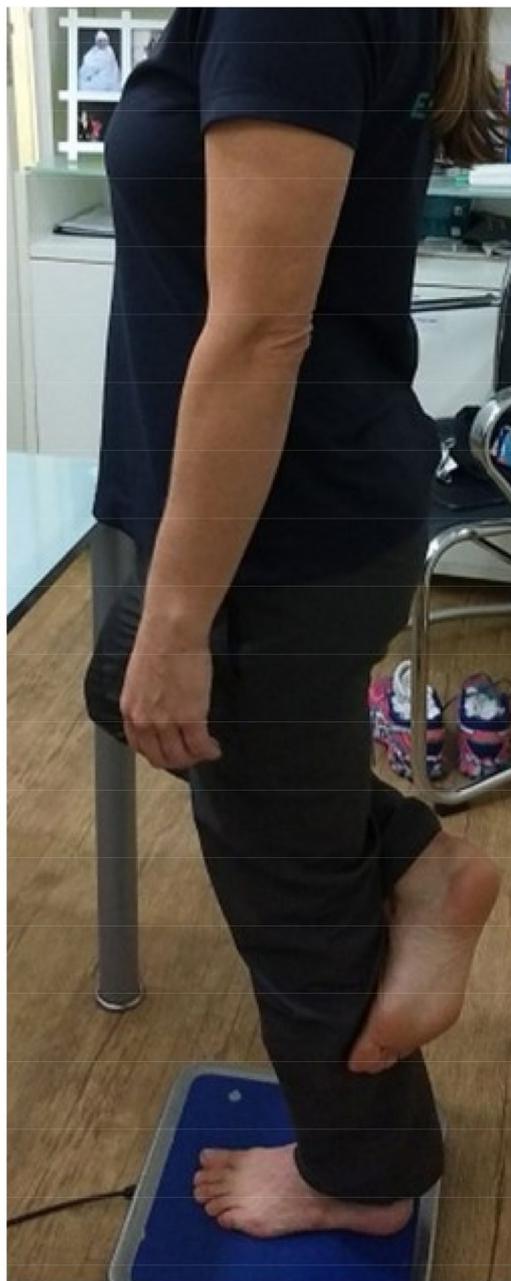
Sex, age, date of evaluation, date of death (if it occurred), censored date and follow-up time were available for all participants. Anthropometric measurements were obtained with participants barefoot and using minimal clothing and included height, weight, sum of six skinfolds—tricipital, subscapular, 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  $\geq 30$  kg/m<sup>2</sup>. 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.<sup>22</sup> 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 $\pm$ 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<sup>23</sup> and Schoenfeld.<sup>24</sup> 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  $\chi^2$  test, after checking, respectively, for the normality of distribution and homogeneity of variance and for the inexistence of expected cell



**Figure 1** Body position to the 10-s one-legged stance test.

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.<sup>25</sup> 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.

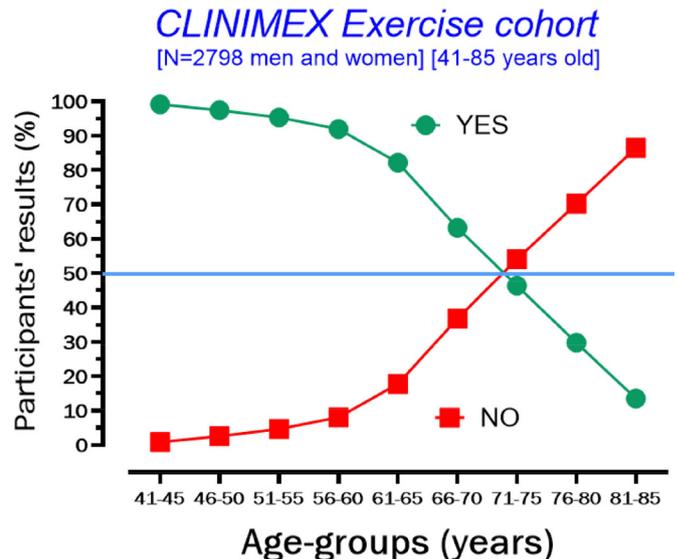
To assess whether adding information on 10-s OLS to conventional risk factors was associated with improvement in the prediction of all-cause mortality, three statistical approaches were employed. First, the improvement in risk discrimination resulting from adding information on 10-s OLS to a model containing established risk factors (age, sex, BMI, medical history of coronary artery disease, hypertension, diabetes and dyslipidaemia) was quantified using Harrell's C-index.<sup>26</sup> 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.<sup>27</sup> 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,<sup>28</sup> 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.<sup>29</sup> In addition to Harrell'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,<sup>30,31</sup> 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.<sup>30,31</sup> 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.

### Patient and public involvement

This research was done without patient or public involvement in the study design, data analysis, writing or editing.

### RESULTS

The mean  $\pm$  SD age of the participants was  $61.7 \pm 6.8$  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



**Figure 2** YES= ability or NO= inability to complete the test to 10-s one-legged stance test according to age groups. This figure includes information from individuals of a wider age range than the one included for analysis in this study as mentioned previously.

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

**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

Variable*	Total (N=1702)	10-s one-leg stance test		P value†
		Yes (n=1354)	No (n=348)	
Age (years)	61.7±6.8	60.3±6.2	67.2±6.0	<0.001
Sex (male)	67.9	68.1	67.2	0.761
Weight (kg)	79.9±16.0	79.0±15.5	83.6±17.3	<0.001
Height (cm)	169.9±9.2	171.1±9.1	169.1±9.6	0.062
Body mass index (kg/m <sup>2</sup> )	27.6±4.5	27.2±4.2	29.2±5.2	<0.001
Waist-height ratio	0.57±0.07	0.56±0.07	0.61±0.08	<0.001
Sum of skinfolds (mm)‡	117.7±1.0	114.6±1.1	129.7±2.4	<0.001
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.

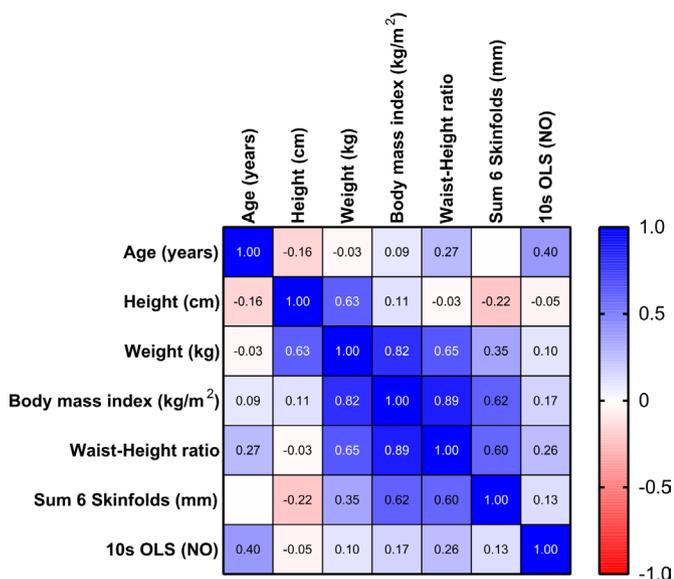
minimally sufficient set of confounders for adjustment is also presented (figure 5).

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

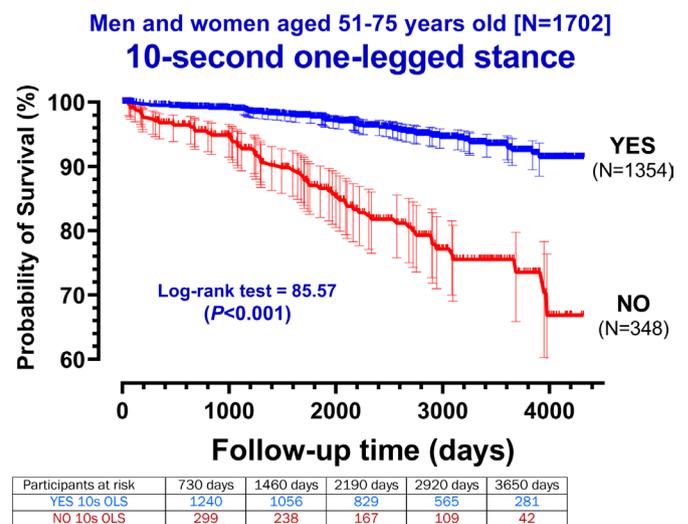
binary results to the model (p for comparison=0.002). The continuous NRI and IDI were 17.50% (95% CI –1.46 to 36.45; p=0.07) and 0.0143 (95% CI 0.0019 to 0.0267; p=0.024), respectively, suggesting additive value of the inability to complete the 10-s OLS test.

**DISCUSSION**

Each year an estimated 684 000 individuals die from falls globally, of which over 80% are in low/middle-income countries.<sup>13</sup> While it is known that good levels of balance are relevant for many daily life activities,<sup>32</sup> there is considerable evidence that



**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 NO) to complete the 10-s one-legged stance test.

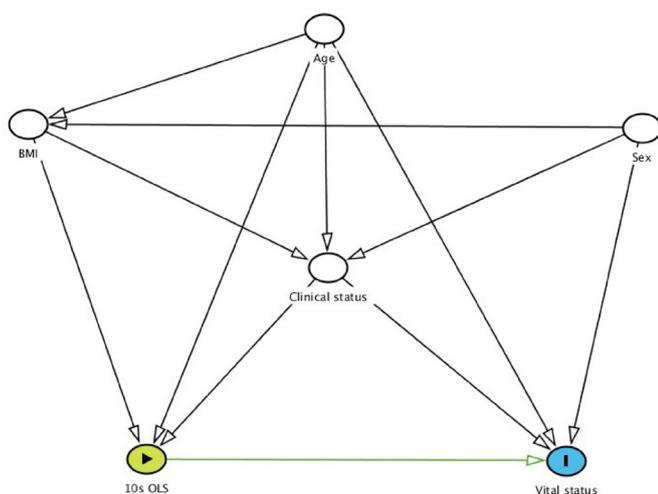
**Table 2** Associations of ability to complete 10-s one-legged stance balance test (10-s OLS) with all-cause mortality in 1702 men and women aged 51–75 years old (123 deaths, 7.2%; median follow-up time=7 years)

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

\*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.

loss of balance is also detrimental for health and that some exercise interventions may improve balance.<sup>12 32–37</sup> However, it 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.<sup>38</sup>

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,<sup>39</sup> the test has been remarkably safe, well-received by the participants, and importantly, simple to



**Figure 5** Directed acyclic graph (DAG) of association between demographic and anthropometric variables, presence of comorbidities, the ability to complete 10-s one-legged stance (10-s OLS) and all-cause mortality. The green box is the exposure variable (10-s OLS). The blue box 'I' is the outcome variable (all-cause mortality). The grey boxes are potential confounding variables. Other potential but unmeasured confounders were omitted from the figure for simplicity. Gender, 10-s OLS, comorbidities, clinical status (healthy or unhealthy) and vital status were used as dichotomous variables. This DAG shows four confounding paths: the path via age, sex, body mass index (BMI) and clinical status (healthy vs unhealthy). Thus, the minimally sufficient adjustment to get the total effect of the exposure on the outcome is to adjust for age, sex, BMI and clinical status.

incorporate in our routine practice as it requires less than 1 or 2 min to be applied.

### 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*<sup>40</sup> 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.<sup>41</sup>

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<sup>15</sup> 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.<sup>15</sup> 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),<sup>22</sup> 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*<sup>42</sup> 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*<sup>16</sup> 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 60s, reflecting the duration that participants were able to maintain the OLS position.<sup>15 16 43–45</sup> While this 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,<sup>46</sup> 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.<sup>18 38 47-49</sup>

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 10s 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 implies a constant relative hazard throughout the follow-up, which is usually not the case.<sup>50</sup> 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

## KEY MESSAGES

### WHAT ARE THE FINDINGS?

⇒ Ability to complete a 10s one-legged stance (10-s OLS) in middle-aged and older participants added relevant prognostic information beyond ordinary clinical data.

### HOW MIGHT IT IMPACT ON CLINICAL PRACTICE IN THE FUTURE?

⇒ 10-s OLS provides rapid and objective feedback for the patient and health professionals regarding static balance.  
 ⇒ The routine application of a simple and safe static balance test—10-s OLS—adds useful information regarding mortality risk in middle-aged and older men and women.

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.

**Correction notice** This article has been corrected since it published Online First. The author's name, Setor Kwadzo Kunutsor, has been amended and affiliations have been updated.

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**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, MFS, JM, SK, JAL. Manuscript writing and revising: all authors. CGA acts as the guarantor of the study.

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**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 CONEP Brazilian Government (reference no: 4.459.555). Participants gave informed consent to participate in the study before taking part.

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

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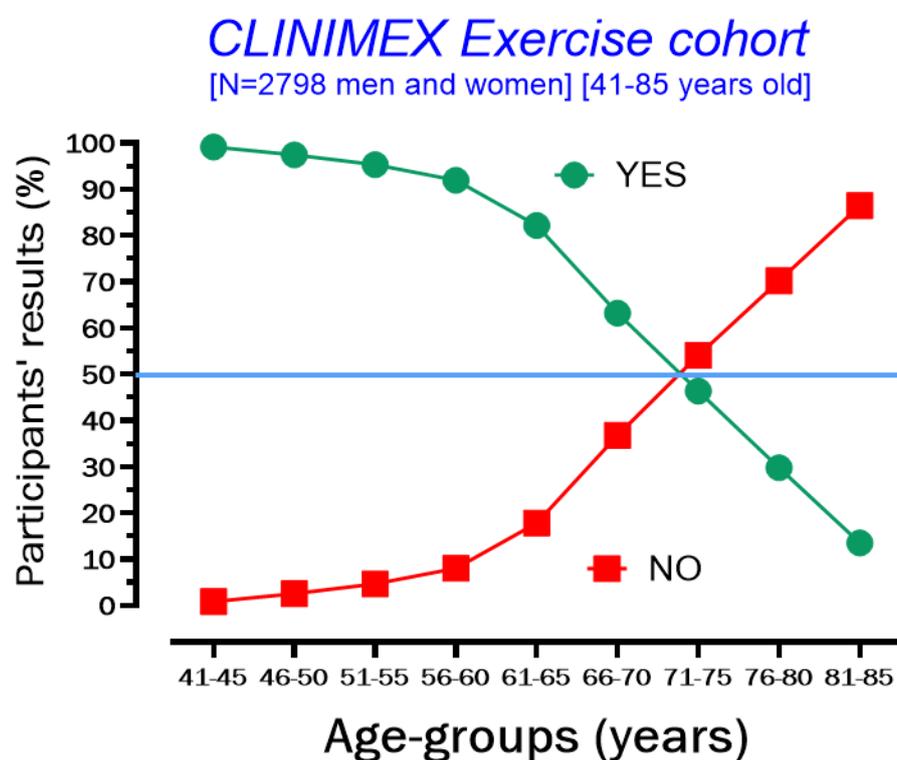
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# SUCCESSFUL 10-SECOND ONE-LEGGED STANCE PERFORMANCE PREDICTS SURVIVAL IN MIDDLE-AGED AND OLDER INDIVIDUALS

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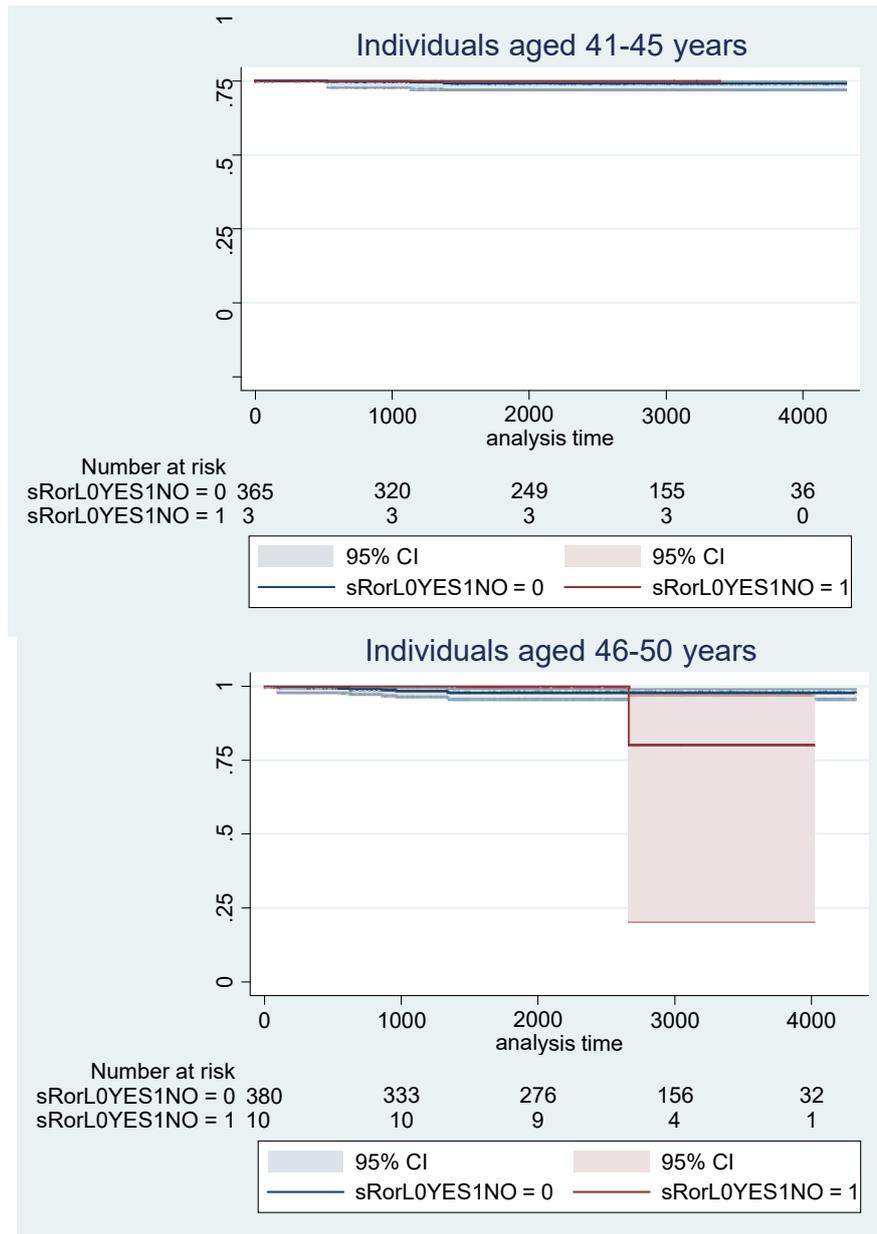
## SUPPLEMENTAL MATERIALS

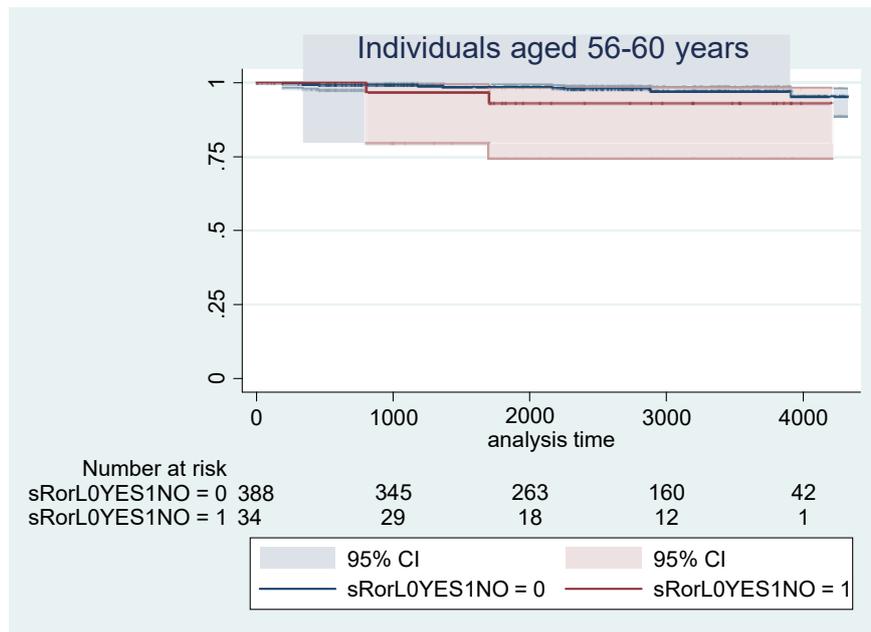
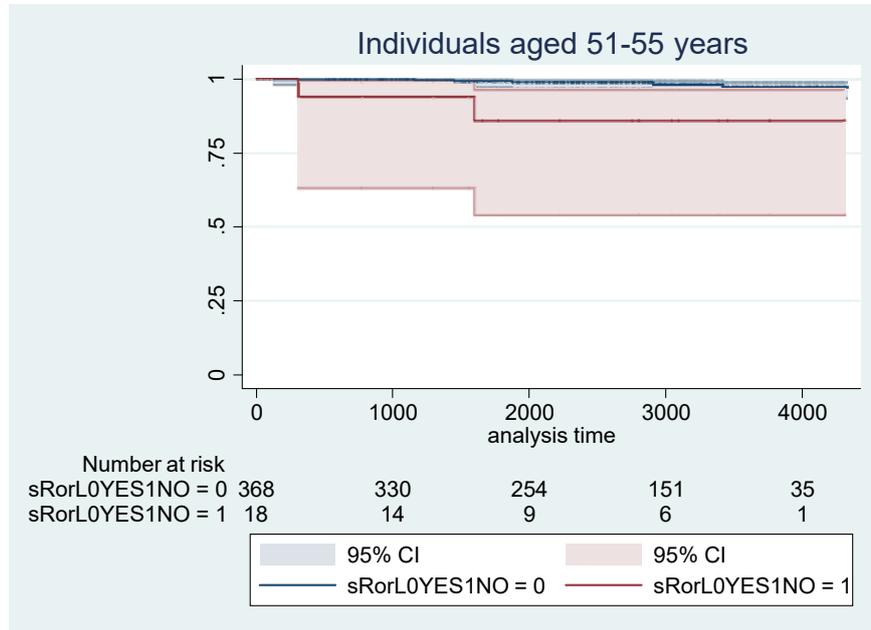
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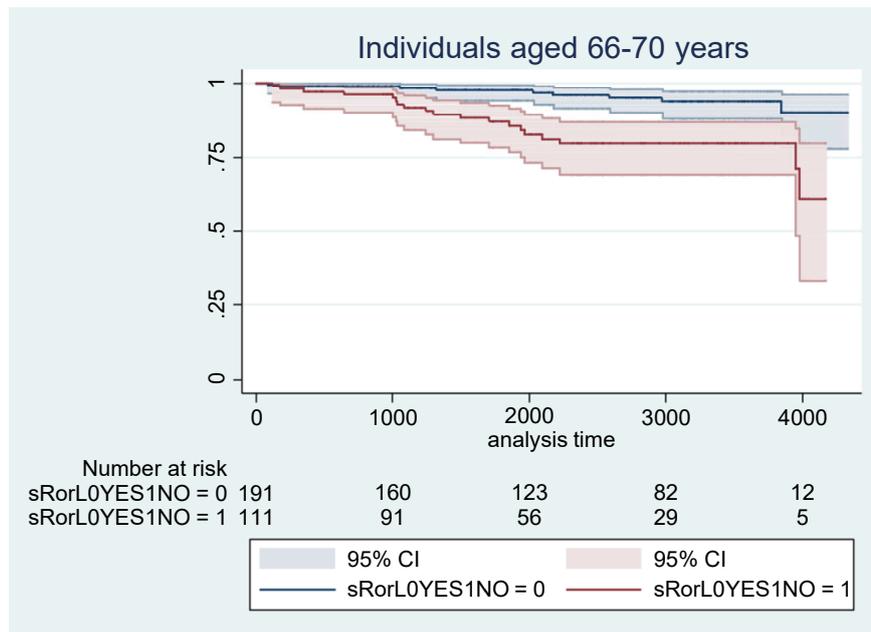
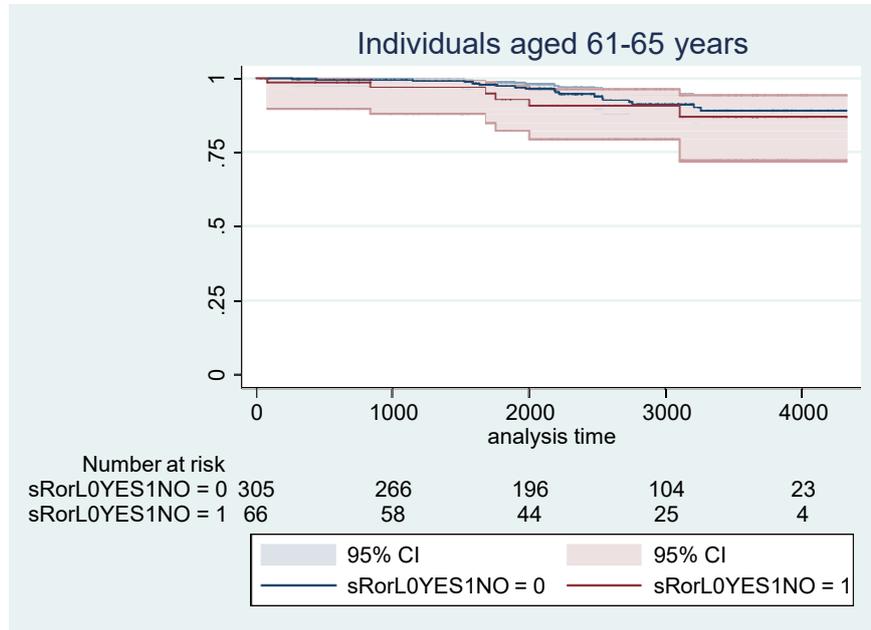


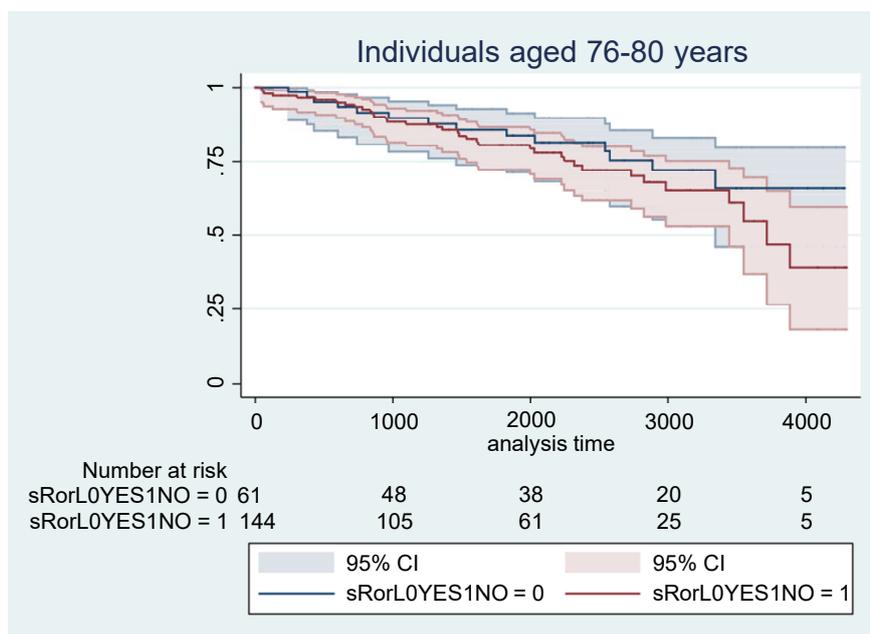
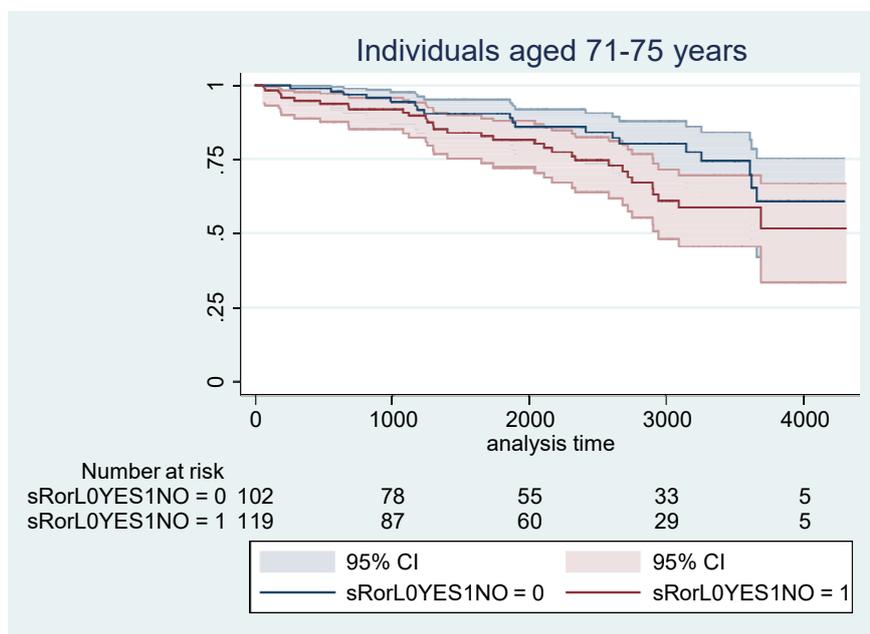
**Figure Suppl 2 (panel with 9 subparts)**

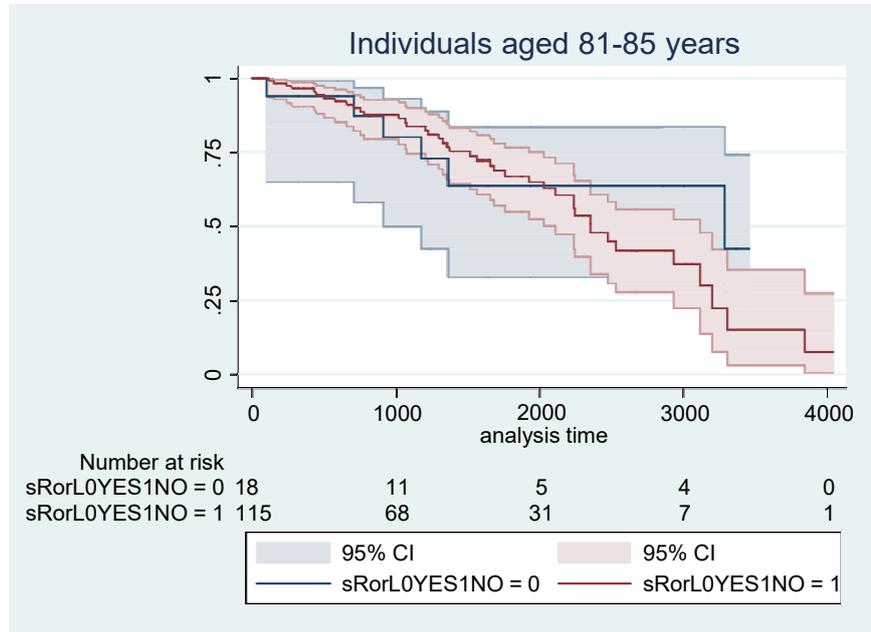
Kaplan-Maier survival curves: 10s one-legged stance test - age ranges: 41-45 years, 46-50 years, 51-55 years, 56-60 years, 61-65 years, 66-70 years, 71-75 years, 76-80 years, 81-85 years





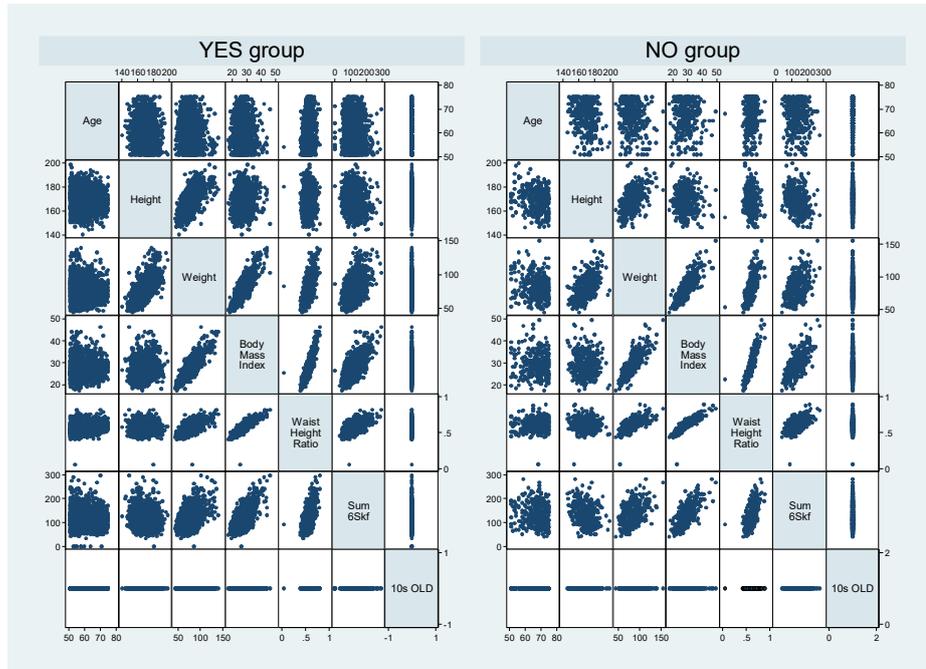






### Figure Suppl 3

Scatterplots with main variables of the study



## CLINIMEX (Exercise Medicine Clinic) Exercise cohort

Since its opening in January 1994, all individuals that were attended at CLINIMEX signed an informed consent specifically allowing that their data, preserved anonymity, could be used for research studies. Evaluation and medically-supervised exercise program (MSEP) protocols, as well as the research proposal, have been repeatedly evaluated and granted approval by different institutional Ethics in Research committees and is also registered at Plataforma Brasil – CONEP.

The CLINIMEX Exercise cohort comprises all the individuals that have been evaluated in our Clinic since its opening in 1994, and, therefore, it is an open cohort. The information is digitally recorded and available for research. It is worthwhile to underscore that all evaluations over these 27 years were conducted by a small team of Exercise & Sports physicians that strictly adhered a rigid protocol.

The illustration below briefly summarizes the cohort status as it was on December 2020.

## Exercise Medicine Clinic



- >9k subjects (1k athletes)
- 2/3 men ( $\pm$  25% healthy)
- Age: 6 to 100 y-old
- Aerobic fitness: 2 to 24 METs
- >13k evaluations (1 to 23)
- 2.5k subjects attended MSEP
- Median f-u 11 years

## *CLINIMEX (Exercise Medicine Clinic) Evaluation Protocol*

The CLINIMEX evaluation protocol consists in several clinical measurements following a strict protocol developed in our Clinic in order to assess aerobic and non-aerobic physical fitness and to advise/prescribe physical exercise.

### Clinical history and physical examination

The CLINIMEX evaluation protocol begins with a detailed anamnesis, which includes the assessment of the individual's patterns of physical activity and exercise/sport in different life spans as follows: 1- childhood and adolescence; 2- adult life; and 3- the last 12 months from the day of the evaluation; and previous participation in competitive sport and in supervised exercise programs. For each one of these life spans, an incremental ordinal score from 0 to 4 is attributed, where 0 refers to sedentary lifestyle, 1 represents insufficiently active [less than minimum recommended dose for age], 2 means achieving the age-recommended dose in terms of regular physical activity, exercise and/or sports, 3 reflects a very active lifestyle [exceeding the minimal recommended dose for age], and 4 is attributed for those that are exceeding the minimal recommended dose in several times and/or are involved in competitive sports that have a high aerobic requirement. Next, a physical examination with an emphasis on the cardiovascular system is performed. Also, information on medications of regular use and results of previous laboratory and complementary exams, when available, are digitally recorded.

### Resting electrocardiogram

Under climatically controlled conditions of temperature (21°C to 24°C) and humidity (40% to 60%), a standard 12-lead resting electrocardiogram in the supine position is registered. During its registration, respiratory sinus arrhythmia is assessed through the measurement of heart rate variation following a slow maximal inspiration and expiration. The ECG recording is obtained and stored using a digital electrocardiograph and specific Wincardio software (Micromed, Brazil).

### Kinanthropometric measurements

Several kinanthropometric measurements are obtained during the CLINIMEX evaluation protocol.

First, basic anthropometry is assessed. Body weight is measured with a Welmy scale, with 0.1 kg resolution; height is measured with a Sanny stadiometer with 0.1 cm resolution; and waist circumference is measured in the upright position, at the umbilicus level, with a Seca or Gullik anthropometric tape with 0.1 cm resolution. Body mass index (kg/m<sup>2</sup>) and waist-height ratio are calculated.

In sequence, skinfolds are measured in six specific sites (medial calf, anterior thigh, triceptal, subscapular, suprailiac and abdominal) using a skinfold caliper (Skyndex or Harpenden, if skinfold >50 mm) at 0.1 mm resolution, bone diameters of humerus and femur are measured by an adapted Mitutoyo caliper with Vernier scale at 0.01 mm, and upper-arm (biceps muscle relaxed and contracted) and calf girths are obtained for calculation of body composition and Heath-Carter anthropometric somatotype.

Next, muscle strength and power are assessed through handgrip strength (absolute and relative to body weight) that is measured twice in both hands with arm completely parallel to the longitudinal axis of the body – the largest result being chosen for subsequent analysis – and maximum power (absolute and relative to body weight) in a standing upright row movement exercise quantified in watts (FitroDyne, Slovakia).

Flexibility is evaluated by applying the Flexitest. Flexitest evaluates the maximal passive range of motion of 20 joint movements. The movement is always initiated at a baseline position towards greater joint amplitude. All the movements are performed passively up to either physical limitation or the individual's complaint of discomfort. For scoring, the range of motion passively obtained for each movement is compared with a reference chart (visual comparison). Discontinuous values ranging from 0 to 4 are assigned to each movement, and no intermediate values are allowed. It is then possible to study the flexibility level in any of 20 individual movements or seven joints. In addition, since flexibility scores for all individual movements present a normal distribution – median of 2 –, it is possible to add them to obtain a global or overall body flexibility dimensionless score, that is called Flexindex (range: 0 to 80). Usually, all movements that are bilateral, by standardization, are performed on the individual's right side.

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### Balance

Balance is assessed in four different positions in a platform (Fitrosway, Slovakia) as follows: 1) double leg stance with feet together and eyes opened; 2) double leg stance with feet together and eyes closed; 3) single leg stance on right foot; 4) and single leg stance on left foot. The individual must be barefoot and he/she must remain on each position for 10 seconds. The center of pressure displacement in all directions during these 10 seconds for each position is determined and recorded by the software.

### Sitting-rising test

The sitting-rising test (SRT) is a safe, costless, quick to apply assessment tool for the evaluation of the four non-aerobic fitness components - flexibility, muscle power, dynamic balance and body composition. The SRT consists in the quantification of the number of supports (hands and/or knees, or hands or forearms on knees) one utilizes in order to sit and to rise from the floor. Independent scores are provided to each of the two actions - sitting and rising. The maximal grade is 5 for each one of the actions, losing one point for each support and additional half point for any detectable unbalance during the performance. A composite score is obtained by adding the sitting and the rising scores, and ranges from 0 to 10 at half point intervals.

### Resting lung spirometry

A standard resting lung spirometry – forced vital capacity and flow-volume curve - is also performed to evaluate the individual's main lung volumes and flows (Schiller [Switzerland] or Koko [United States] spirometers). The maneuver that achieves the highest sum of forced vital capacity and forced expiratory volume at the first second from three high-quality maneuvers is chosen to represent the individual's results.

### The 4-Second Exercise Test

The aim of the 4-Second Exercise Test (4sET) is to assess the integrity of the cardiac parasympathetic branch of the autonomic nervous system in the initial transient of heart rate

(rest-exercise transition) and is based on the physiological vagal withdrawal induced by movement of the limbs. Briefly, the 4sET consists of cycling, as fast as possible, an unloaded cycloergometer, from the fifth to the ninth second of a maximum inspiratory apnea lasting 12 seconds. The individual being tested should follow four verbal commands at each 4 seconds: a) to get a maximal quick full inspiration, primarily through the mouth; b) to cycle as fast as possible; c) to stop abruptly; and d) to expire normally. During this test, a single electrocardiographic tracing is continuously recorded (usually lead CC5 or CM5) during 35 seconds, at a velocity of 25 mm/s that is initiated 5 seconds before the maximum inspiration command. To determine the magnitude of the cardiac vagal tone, the longest RR interval – the one immediately before, or the first during exercise, whatever is the largest one – and the shortest RR interval during exercise – usually the last one – are identified and measured at 10 ms resolution in the digital tracing. The ratio between these two RR interval durations indicates the cardiac vagal index, a dimensionless variable that is obtained by the 4sET. If a longer RR interval duration is detected after the exhalation, it is also recorded and it reflects a vagal rebound phenomena.

#### Cardiopulmonary exercise test (CPX)

CPX is conducted in a room that is adequately prepared – personnel, equipments, medications and supplies - to handle with medical emergencies that may arise. While both cycling and treadmill CPX could be performed at CLINIMEX, the vast majority of our CPX are undertaken in a lower limb cycle ergometer Cateye EC-1600 (Cateye, Japan) or Inbrasport CG-04 (Inbrasport, Brazil). When appropriate, mostly in exercisers or athletes used to run, CPX is performed on an Inbrasport ATL-2000 treadmill (Inbrasport, Brazil). Very rarely and for specific reasons, a Monark upper limb cycle ergometer (Monark, Sweden) or an Inbrasport arm ergometer (Inbrasport, Brazil) or a Concept II remoergometer (Concept, United States) are used for CPX. For all CPX, expired gases are collected by the use of a Prevent pneumotacograph (MedGraphics, USA) coupled to a mouthpiece, with concomitant nasal occlusion. The expired gases are measured and analyzed by using a VO<sub>2000</sub> metabolic analyzer (MedGraphics, USA) daily calibrated for volumes and gas fractions before the first assessment and whenever necessary. Using a mixed chamber concept, expired gases are averaged and read every 10 seconds. For simplicity, these 10-second results are, subsequently, averaged for each minute.

During the CPX, the individual is continuously monitored from resting until five minutes after exercise is completed with a digital electrocardiograph (ErgoPC Elite, versions 3.2.1.5 or 3.3.4.3 or 3.3.6.2, Micromed, Brazil). Heart rate is measured on the electrocardiographic recording (leads CC5 or CM5) at the end of each minute. Blood pressure is measured by

physician's auscultation every minute on the right arm by using a manual sphygmomanometer during exercise and in the first, second, third and fifth minute of recovery (most frequently on the supine position). After being previously explained to the individual, rate of overall perceived exertion in an ordinal incremental scale from 0 to 10 (half-point allowed) is asked at each minute by the physician in charge to the individual and also recorded.

The CPX is always performed according to an individualized ramp protocol, aimed to achieve voluntary exhaustion at 8 to 12 minute duration. The maximum intensity of the exercise is confirmed by maximum voluntary exhaustion (score 10 in the Borg scale ranging from 0 to 10) represented by the incapacity to continue the effort despite strong verbal encouragement. The characterization of CPX as maximum is also confirmed by the impression of the physician in charge and recorded on the CPX's report. CPX is neither interrupted nor considered maximum based exclusively on the heart rate achieved.

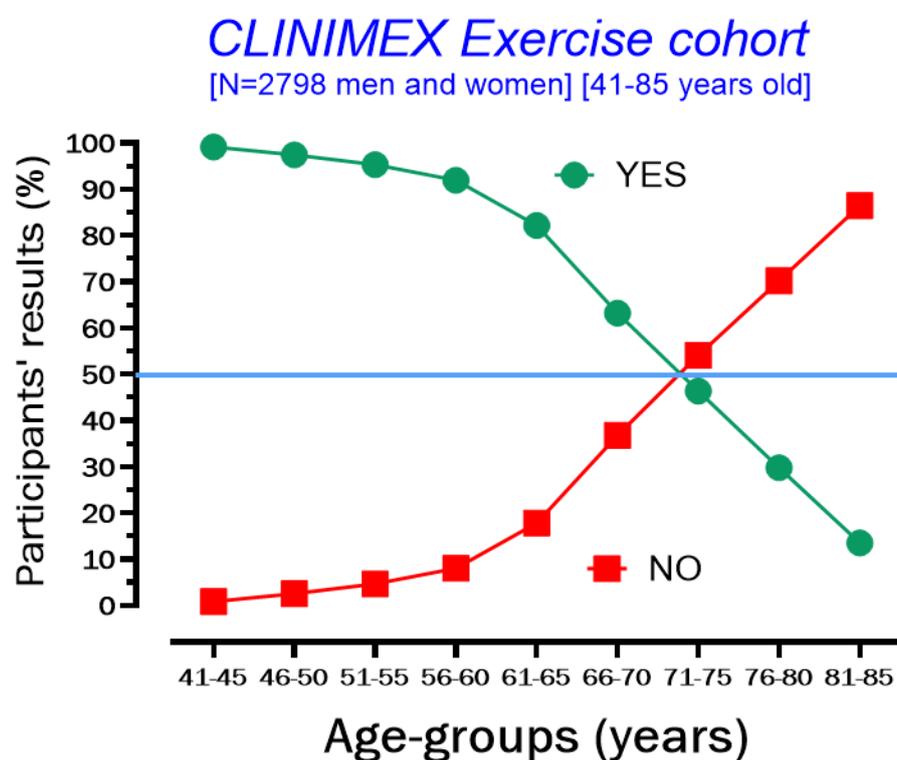
The following variables are also obtained from the CPX: 1- maximum oxygen uptake ( $\text{VO}_2\text{max}$ ): the highest oxygen uptake value obtained at a given minute of the CPX and expressed as absolute ( $\text{L}\cdot\text{min}^{-1}$ ) or relative to body weight ( $\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ) value or as percent of maximal sex- and age-predicted value – men:  $60 - 0.55 \times \text{age}$  in years and women:  $48 - 0.37 \times \text{age}$  in years -; 2- anaerobic threshold (in  $\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$  or % of  $\text{VO}_2\text{max}$ ), determined based on the graphical inspection of data on oxygen consumption ( $\text{VO}_2$ ) and ventilation (VE), at which point there is a sudden loss in the linearity of VE curve, whereas  $\text{VO}_2$  continues to increase linearly with the workload; 3-  $\text{O}_2$  pulse (absolute or per body weight unit), calculated as  $\text{VO}_2/\text{heart rate}$  ratio obtained every 10 seconds; 4- Cardiorespiratory optimal point, a dimensionless variable, obtained by identifying the lowest value of the  $\text{VE}/\text{VO}_2$  ratio measured minute-by-minute during the incremental maximum CPX, regardless of when it occurred; 5- Exercise heart rate gradient (EHRG), an index combining heart rate reserve (maximum heart rate minus heart rate at rest) and heart rate recovery (maximum heart rate minus heart rate one minute post exercise); 6- Oxygen saturation, measured by plethysmography using a finger oxymeter and recorded minute-by-minute during exercise and in the first five minutes of post-exercise period of CPX. Additionally, curve kinetics for all variables is also evaluated.

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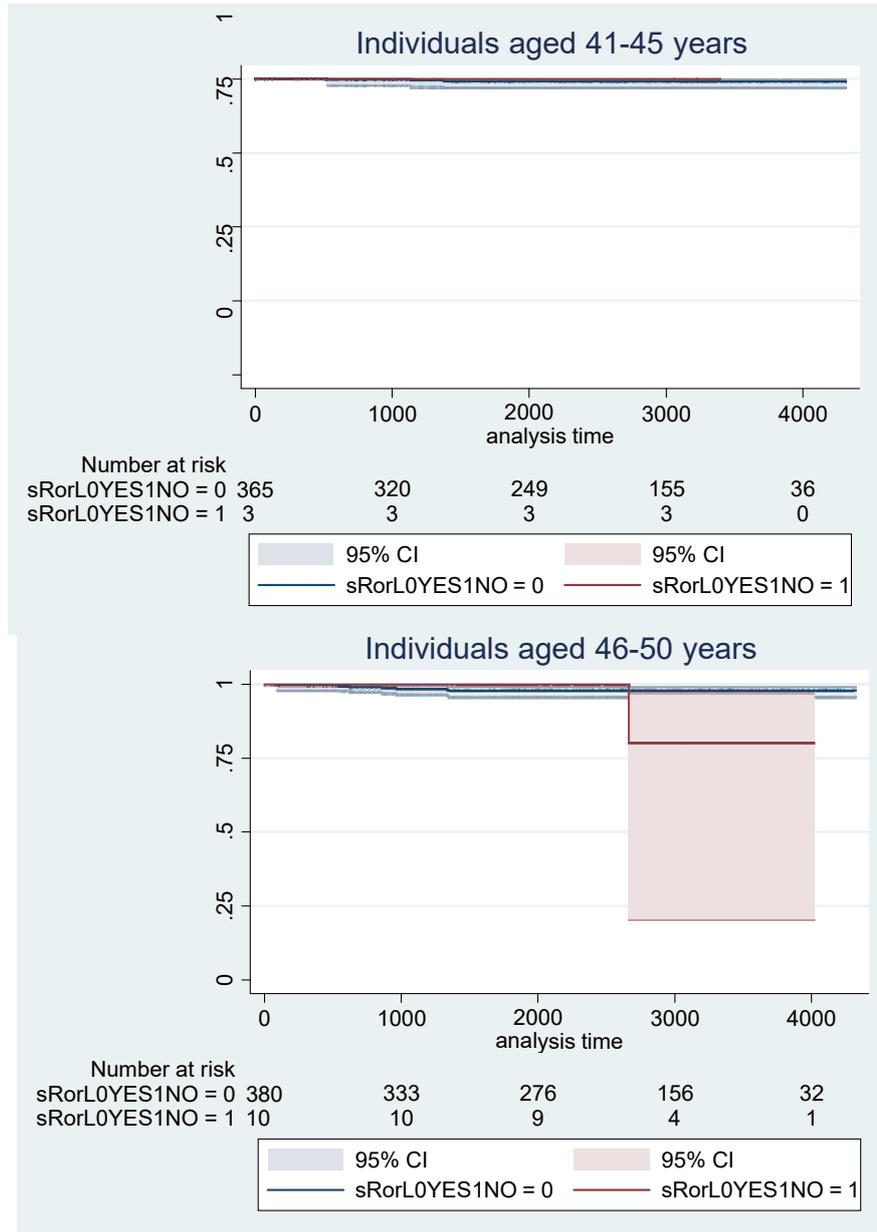
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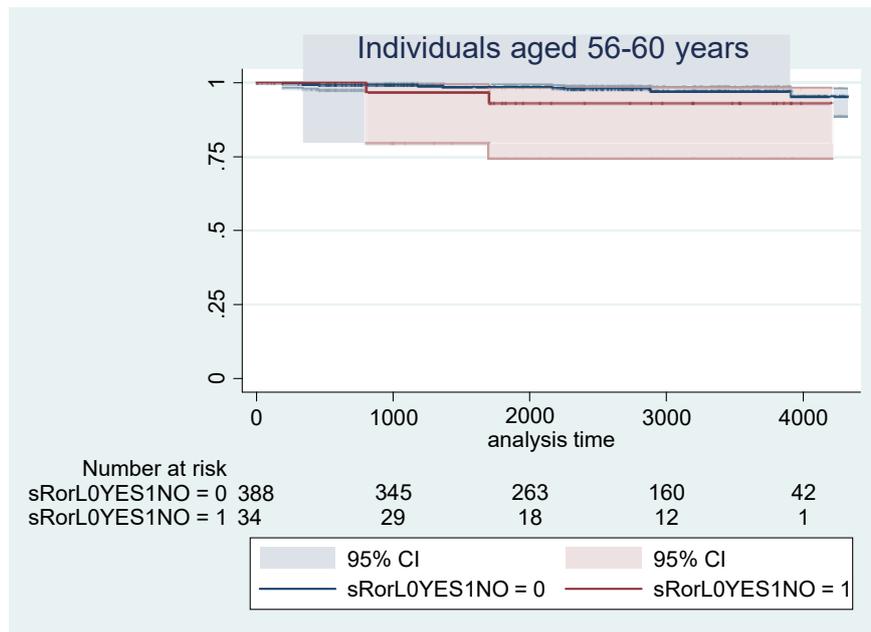
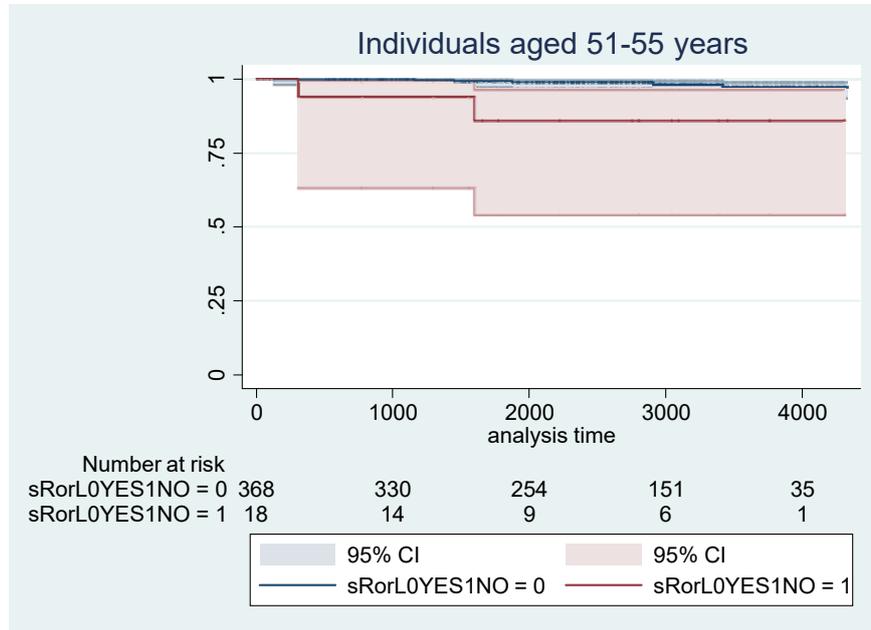
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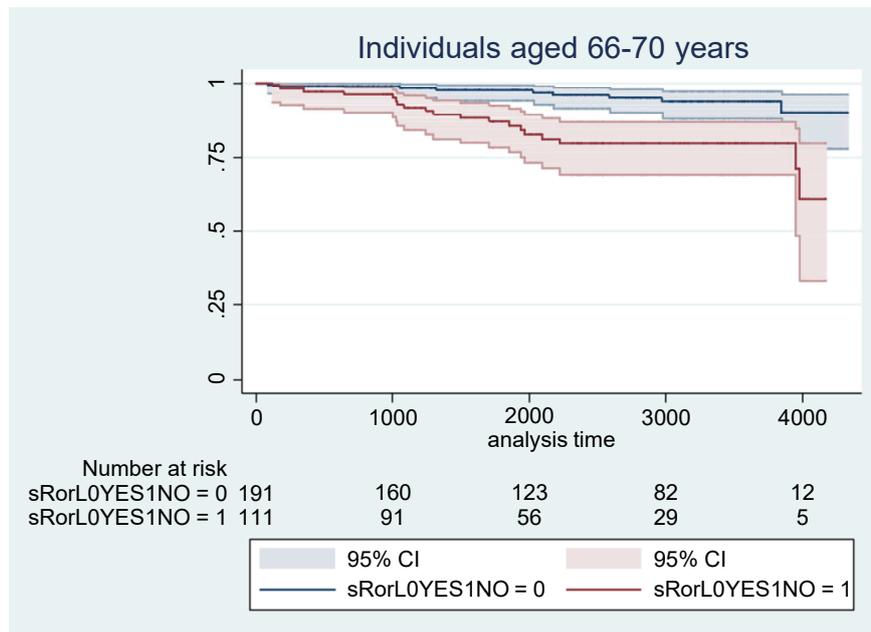
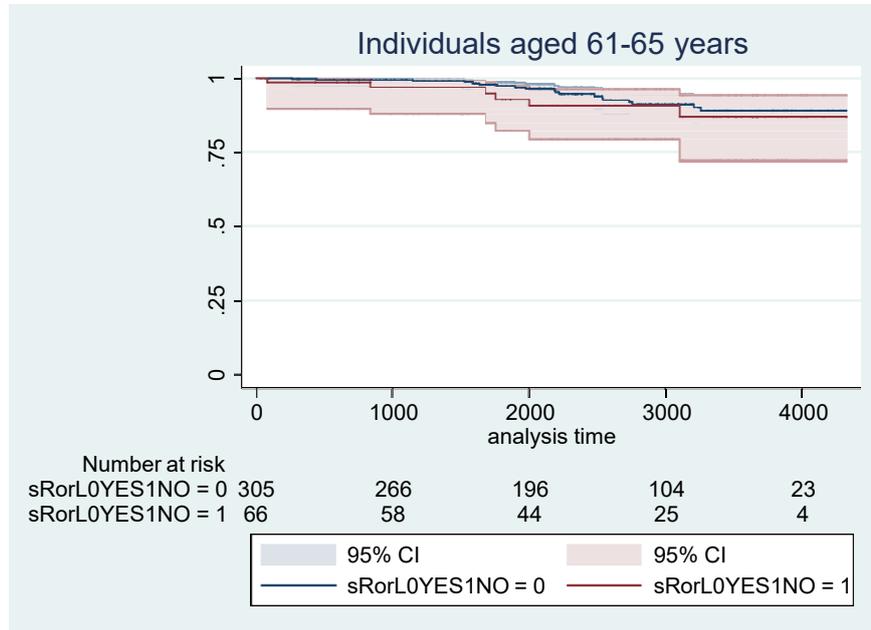


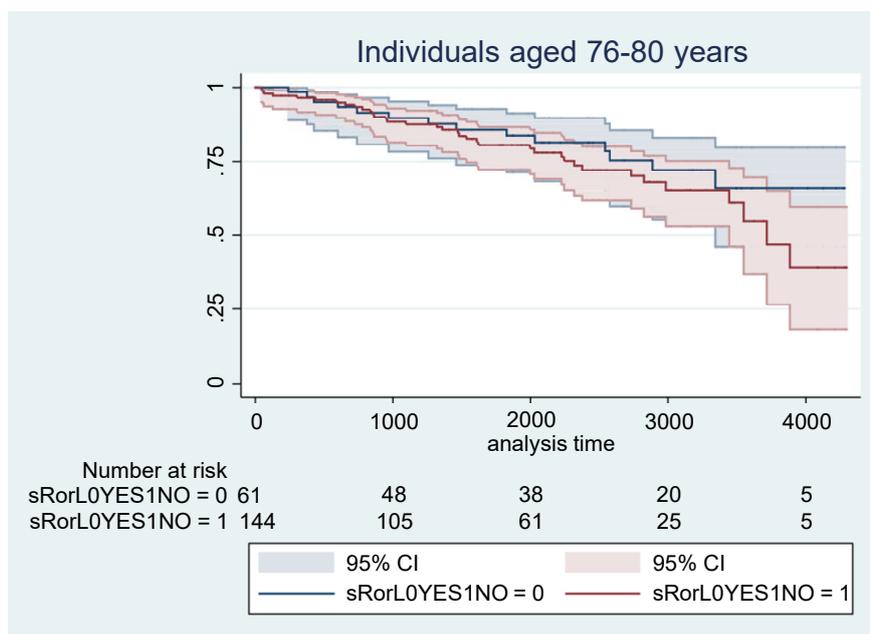
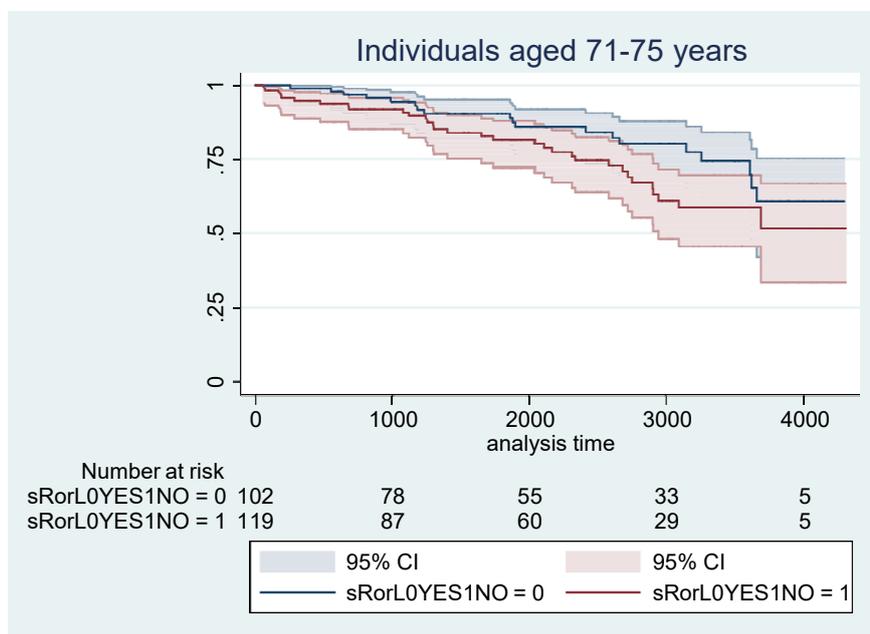
**Figure Suppl 2 (panel with 9 subparts)**

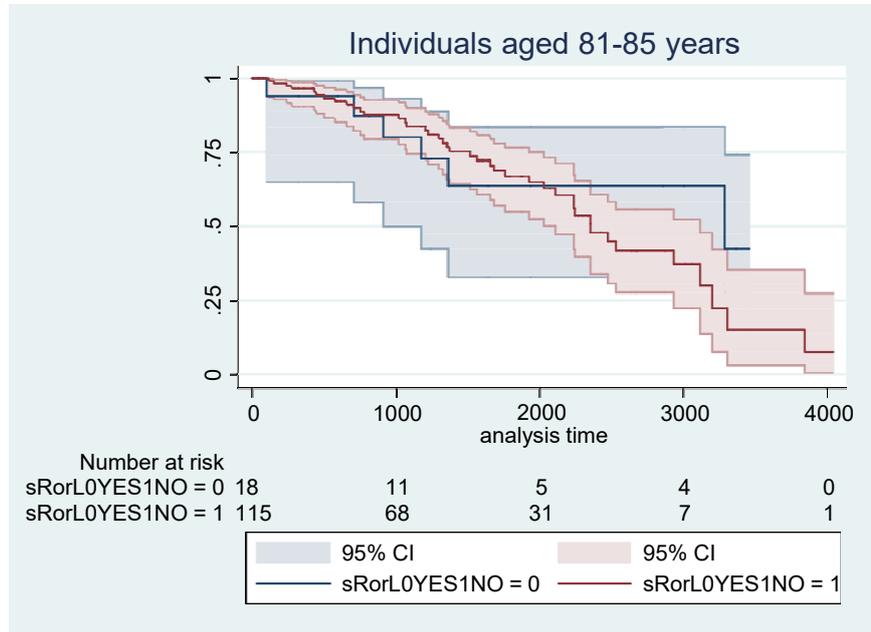
Kaplan-Maier survival curves: 10s one-legged stance test - age ranges: 41-45 years, 46-50 years, 51-55 years, 56-60 years, 61-65 years, 66-70 years, 71-75 years, 76-80 years, 81-85 years





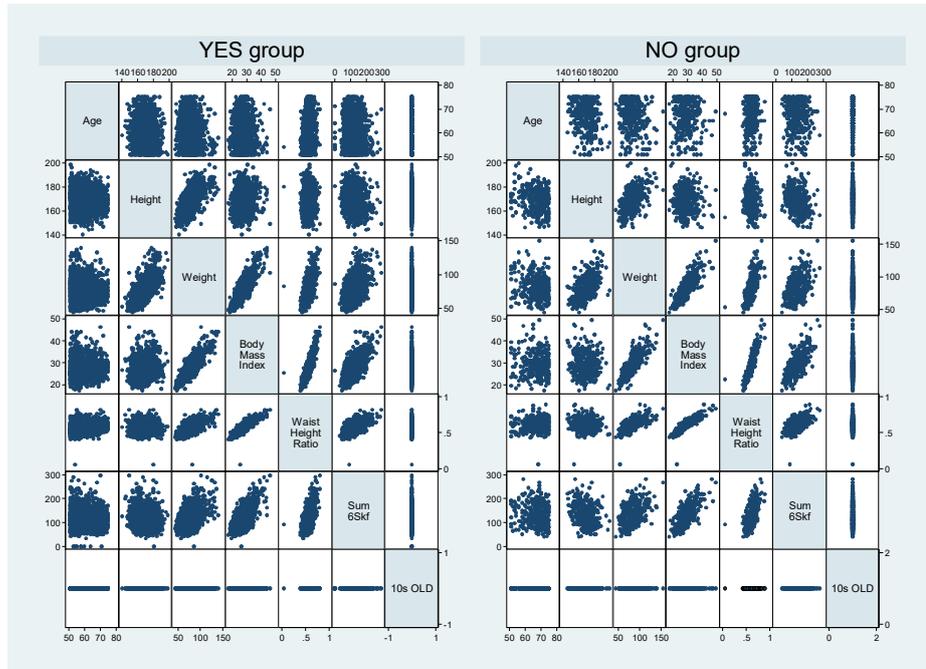






### Figure Suppl 3

Scatterplots with main variables of the study



## CLINIMEX (Exercise Medicine Clinic) Exercise cohort

Since its opening in January 1994, all individuals that were attended at CLINIMEX signed an informed consent specifically allowing that their data, preserved anonymity, could be used for research studies. Evaluation and medically-supervised exercise program (MSEP) protocols, as well as the research proposal, have been repeatedly evaluated and granted approval by different institutional Ethics in Research committees and is also registered at Plataforma Brasil – CONEP.

The CLINIMEX Exercise cohort comprises all the individuals that have been evaluated in our Clinic since its opening in 1994, and, therefore, it is an open cohort. The information is digitally recorded and available for research. It is worthwhile to underscore that all evaluations over these 27 years were conducted by a small team of Exercise & Sports physicians that strictly adhered a rigid protocol.

The illustration below briefly summarizes the cohort status as it was on December 2020.

## Exercise Medicine Clinic



- >9k subjects (1k athletes)
- 2/3 men ( $\pm$  25% healthy)
- Age: 6 to 100 y-old
- Aerobic fitness: 2 to 24 METs
- >13k evaluations (1 to 23)
- 2.5k subjects attended MSEP
- Median f-u 11 years

## *CLINIMEX (Exercise Medicine Clinic) Evaluation Protocol*

The CLINIMEX evaluation protocol consists in several clinical measurements following a strict protocol developed in our Clinic in order to assess aerobic and non-aerobic physical fitness and to advise/prescribe physical exercise.

### Clinical history and physical examination

The CLINIMEX evaluation protocol begins with a detailed anamnesis, which includes the assessment of the individual's patterns of physical activity and exercise/sport in different life spans as follows: 1- childhood and adolescence; 2- adult life; and 3- the last 12 months from the day of the evaluation; and previous participation in competitive sport and in supervised exercise programs. For each one of these life spans, an incremental ordinal score from 0 to 4 is attributed, where 0 refers to sedentary lifestyle, 1 represents insufficiently active [less than minimum recommended dose for age], 2 means achieving the age-recommended dose in terms of regular physical activity, exercise and/or sports, 3 reflects a very active lifestyle [exceeding the minimal recommended dose for age], and 4 is attributed for those that are exceeding the minimal recommended dose in several times and/or are involved in competitive sports that have a high aerobic requirement. Next, a physical examination with an emphasis on the cardiovascular system is performed. Also, information on medications of regular use and results of previous laboratory and complementary exams, when available, are digitally recorded.

### Resting electrocardiogram

Under climatically controlled conditions of temperature (21°C to 24°C) and humidity (40% to 60%), a standard 12-lead resting electrocardiogram in the supine position is registered. During its registration, respiratory sinus arrhythmia is assessed through the measurement of heart rate variation following a slow maximal inspiration and expiration. The ECG recording is obtained and stored using a digital electrocardiograph and specific Wincardio software (Micromed, Brazil).

### Kinanthropometric measurements

Several kinanthropometric measurements are obtained during the CLINIMEX evaluation protocol.

First, basic anthropometry is assessed. Body weight is measured with a Welmy scale, with 0.1 kg resolution; height is measured with a Sanny stadiometer with 0.1 cm resolution; and waist circumference is measured in the upright position, at the umbilicus level, with a Seca or Gullik anthropometric tape with 0.1 cm resolution. Body mass index (kg/m<sup>2</sup>) and waist-height ratio are calculated.

In sequence, skinfolds are measured in six specific sites (medial calf, anterior thigh, triceptal, subscapular, suprailiac and abdominal) using a skinfold caliper (Skyndex or Harpenden, if skinfold >50 mm) at 0.1 mm resolution, bone diameters of humerus and femur are measured by an adapted Mitutoyo caliper with Vernier scale at 0.01 mm, and upper-arm (biceps muscle relaxed and contracted) and calf girths are obtained for calculation of body composition and Heath-Carter anthropometric somatotype.

Next, muscle strength and power are assessed through handgrip strength (absolute and relative to body weight) that is measured twice in both hands with arm completely parallel to the longitudinal axis of the body – the largest result being chosen for subsequent analysis – and maximum power (absolute and relative to body weight) in a standing upright row movement exercise quantified in watts (FitroDyne, Slovakia).

Flexibility is evaluated by applying the Flexitest. Flexitest evaluates the maximal passive range of motion of 20 joint movements. The movement is always initiated at a baseline position towards greater joint amplitude. All the movements are performed passively up to either physical limitation or the individual's complaint of discomfort. For scoring, the range of motion passively obtained for each movement is compared with a reference chart (visual comparison). Discontinuous values ranging from 0 to 4 are assigned to each movement, and no intermediate values are allowed. It is then possible to study the flexibility level in any of 20 individual movements or seven joints. In addition, since flexibility scores for all individual movements present a normal distribution – median of 2 –, it is possible to add them to obtain a global or overall body flexibility dimensionless score, that is called Flexindex (range: 0 to 80). Usually, all movements that are bilateral, by standardization, are performed on the individual's right side.

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### Balance

Balance is assessed in four different positions in a platform (Fitrosway, Slovakia) as follows: 1) double leg stance with feet together and eyes opened; 2) double leg stance with feet together and eyes closed; 3) single leg stance on right foot; 4) and single leg stance on left foot. The individual must be barefoot and he/she must remain on each position for 10 seconds. The center of pressure displacement in all directions during these 10 seconds for each position is determined and recorded by the software.

### Sitting-rising test

The sitting-rising test (SRT) is a safe, costless, quick to apply assessment tool for the evaluation of the four non-aerobic fitness components - flexibility, muscle power, dynamic balance and body composition. The SRT consists in the quantification of the number of supports (hands and/or knees, or hands or forearms on knees) one utilizes in order to sit and to rise from the floor. Independent scores are provided to each of the two actions - sitting and rising. The maximal grade is 5 for each one of the actions, losing one point for each support and additional half point for any detectable unbalance during the performance. A composite score is obtained by adding the sitting and the rising scores, and ranges from 0 to 10 at half point intervals.

### Resting lung spirometry

A standard resting lung spirometry – forced vital capacity and flow-volume curve - is also performed to evaluate the individual's main lung volumes and flows (Schiller [Switzerland] or Koko [United States] spirometers). The maneuver that achieves the highest sum of forced vital capacity and forced expiratory volume at the first second from three high-quality maneuvers is chosen to represent the individual's results.

### The 4-Second Exercise Test

The aim of the 4-Second Exercise Test (4sET) is to assess the integrity of the cardiac parasympathetic branch of the autonomic nervous system in the initial transient of heart rate

(rest-exercise transition) and is based on the physiological vagal withdrawal induced by movement of the limbs. Briefly, the 4sET consists of cycling, as fast as possible, an unloaded cycloergometer, from the fifth to the ninth second of a maximum inspiratory apnea lasting 12 seconds. The individual being tested should follow four verbal commands at each 4 seconds: a) to get a maximal quick full inspiration, primarily through the mouth; b) to cycle as fast as possible; c) to stop abruptly; and d) to expire normally. During this test, a single electrocardiographic tracing is continuously recorded (usually lead CC5 or CM5) during 35 seconds, at a velocity of 25 mm/s that is initiated 5 seconds before the maximum inspiration command. To determine the magnitude of the cardiac vagal tone, the longest RR interval – the one immediately before, or the first during exercise, whatever is the largest one – and the shortest RR interval during exercise – usually the last one – are identified and measured at 10 ms resolution in the digital tracing. The ratio between these two RR interval durations indicates the cardiac vagal index, a dimensionless variable that is obtained by the 4sET. If a longer RR interval duration is detected after the exhalation, it is also recorded and it reflects a vagal rebound phenomena.

#### Cardiopulmonary exercise test (CPX)

CPX is conducted in a room that is adequately prepared – personnel, equipments, medications and supplies - to handle with medical emergencies that may arise. While both cycling and treadmill CPX could be performed at CLINIMEX, the vast majority of our CPX are undertaken in a lower limb cycle ergometer Cateye EC-1600 (Cateye, Japan) or Inbrasport CG-04 (Inbrasport, Brazil). When appropriate, mostly in exercisers or athletes used to run, CPX is performed on an Inbrasport ATL-2000 treadmill (Inbrasport, Brazil). Very rarely and for specific reasons, a Monark upper limb cycle ergometer (Monark, Sweden) or an Inbrasport arm ergometer (Inbrasport, Brazil) or a Concept II remoergometer (Concept, United States) are used for CPX. For all CPX, expired gases are collected by the use of a Prevent pneumotacograph (MedGraphics, USA) coupled to a mouthpiece, with concomitant nasal occlusion. The expired gases are measured and analyzed by using a VO<sub>2000</sub> metabolic analyzer (MedGraphics, USA) daily calibrated for volumes and gas fractions before the first assessment and whenever necessary. Using a mixed chamber concept, expired gases are averaged and read every 10 seconds. For simplicity, these 10-second results are, subsequently, averaged for each minute.

During the CPX, the individual is continuously monitored from resting until five minutes after exercise is completed with a digital electrocardiograph (ErgoPC Elite, versions 3.2.1.5 or 3.3.4.3 or 3.3.6.2, Micromed, Brazil). Heart rate is measured on the electrocardiographic recording (leads CC5 or CM5) at the end of each minute. Blood pressure is measured by

physician's auscultation every minute on the right arm by using a manual sphygmomanometer during exercise and in the first, second, third and fifth minute of recovery (most frequently on the supine position). After being previously explained to the individual, rate of overall perceived exertion in an ordinal incremental scale from 0 to 10 (half-point allowed) is asked at each minute by the physician in charge to the individual and also recorded.

The CPX is always performed according to an individualized ramp protocol, aimed to achieve voluntary exhaustion at 8 to 12 minute duration. The maximum intensity of the exercise is confirmed by maximum voluntary exhaustion (score 10 in the Borg scale ranging from 0 to 10) represented by the incapacity to continue the effort despite strong verbal encouragement. The characterization of CPX as maximum is also confirmed by the impression of the physician in charge and recorded on the CPX's report. CPX is neither interrupted nor considered maximum based exclusively on the heart rate achieved.

The following variables are also obtained from the CPX: 1- maximum oxygen uptake ( $\text{VO}_2\text{max}$ ): the highest oxygen uptake value obtained at a given minute of the CPX and expressed as absolute ( $\text{L}\cdot\text{min}^{-1}$ ) or relative to body weight ( $\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ) value or as percent of maximal sex- and age-predicted value – men:  $60 - 0.55 \times \text{age}$  in years and women:  $48 - 0.37 \times \text{age}$  in years -; 2- anaerobic threshold (in  $\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$  or % of  $\text{VO}_2\text{max}$ ), determined based on the graphical inspection of data on oxygen consumption ( $\text{VO}_2$ ) and ventilation (VE), at which point there is a sudden loss in the linearity of VE curve, whereas  $\text{VO}_2$  continues to increase linearly with the workload; 3-  $\text{O}_2$  pulse (absolute or per body weight unit), calculated as  $\text{VO}_2/\text{heart rate}$  ratio obtained every 10 seconds; 4- Cardiorespiratory optimal point, a dimensionless variable, obtained by identifying the lowest value of the VE/ $\text{VO}_2$  ratio measured minute-by-minute during the incremental maximum CPX, regardless of when it occurred; 5- Exercise heart rate gradient (EHRG), an index combining heart rate reserve (maximum heart rate minus heart rate at rest) and heart rate recovery (maximum heart rate minus heart rate one minute post exercise); 6- Oxygen saturation, measured by plethysmography using a finger oxymeter and recorded minute-by-minute during exercise and in the first five minutes of post-exercise period of CPX. Additionally, curve kinetics for all variables is also evaluated.