Peak oxygen pulse response during maximal cardiopulmonary exercise testing on a treadmill: applicability analysis of the FRIEND registry prediction equation in a Brazilian healthy sample

G. Cipriano Junior[1], M. Milani[1], J.G.P.O. Milani[1], G.F.B. Cipriano[1], D. Hansen[2], J. Myers[3]

[1]University of Brasilia, Health Sciences and Technologies Graduate Program, Brasilia, Brazil
[2]Hasselt University, Faculty of Rehabilitation Sciences, Hasselt, Belgium
[3]Palo Alto VAHCS Veteran Centre, Palo Alto, United States of America

Background: Peak oxygen uptake (VO2peak), measured by cardiopulmonary exercise test (CPET), is an established variable for prognostic assessment. Other VO2peak-derived variables, such as the peak oxygen pulse (peakO2pulse), also provide valuable information for risk stratification in patients with cardiac diseases. For individualized assessment, the measured peakO2pulse can be compared to reference standards using predictive equations, such as the FRIEND Registry [peakO2pulse = $23.2 - (0.09 \times Age) - (6.6 \times Sex$ (female:1; male: 0))]. However, the applicabilty of this equation in a Brazilian population sample has never been evaluated.

Purpose: To conduct an external validation of the FRIEND registry prediction equation for treadmill peakO2pulse in a sample of healthy Brazilian individuals.

Methods: Cross-sectional study involving subjects assessed by treadmill CPET in the Brazilian Midwest region from January 2011 to March 2020. Inclusion criteria: healthy individuals aged $\geq$ 20 years with a peak respiratory exchange ratio $\geq$ 1.00. Exclusion criteria: history of cardiovascular or pulmonary disease, presence of cardiovascular risk factors (hypertension, diabetes mellitus, current smoking, and obesity), and abnormalities on CPET. Variables were described as median and interquartile range (IQR). Statistical comparisons between measured and predicted values were conducted using the Wilcoxon signed rank test, including the calculation of the median differences and the 95% confidence interval (CI). Furthermore, Bland-Altman agreement analysis was utilized to assess the concordance between measured and estimated values.

Results: A total of 7,843 CPETs were performed. After applying inclusion and exclusion criteria, 3,544 assessments were included (1,574 females and 1,970 males) aged between 20 to 80 years. In the females, the median and IQR of measured peakO2pulse and predicted values were 10.4 (9.0; 12.1) and 13.1 (12.3; 13.7) ml/beat, respectively. This difference was statistically significant ($p < 0.001$), with a median difference of 2.54 mL/beat (95% CI: 2.40; 2.69). For males, the measured and predicted values were 17.3 (15.1; 19.7) and 19.7 (19.0; 20.2) ml/beat, respectively. The median difference was statistically significant at 2.26 mL/beat (95% CI: 2.11; 2.46) ($p < 0.001$) (Figure 1). Bland-Altman agreement analysis indicated a bias of 2.33 mL/beat (95% limits of agreement: -2.17 to 6.83) in females and 2.15 mL/beat (95% limits of agreement: -4.34 to 8.65) in males (Figure 2).

Conclusions: The study reveals that measured median peakO2pulse values are consistently lower than predicted across both sexes, highlighting a significant bias, which limits the applicability of the FRIEND registry prediction equation in the Brazilian population and underscores the international heterogeneity of the variable. The findings advocate for the development of region-specific reference standards to enhance accuracy in predicting peakO2pulse values.

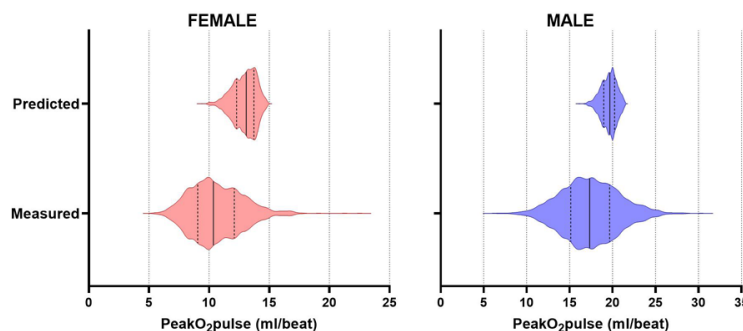Figure 1.Box plots of measured and predicted peak oxygen pulse.

Figure 2. Bland-Altman plots of measured and predicted peak oxygen pulse.