Accuracy of Predictive Equations for Maximal Oxygen Consumption in Healthy Native and Acclimatized Young Adults Living at Moderate Altitude

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INTRODUCTION

Maximal oxygen consumption ($VO_{2\,max}$) is the gold standard for evaluation of cardiorespiratory fitness. Predictive equations for $VO_{2\,max}$ serve as reference for performing cardiopulmonary exercise testing (CPET) and for exercise prescription in settings in which direct $VO_{2\,max}$ measurement is not feasible [1].

About 8 million people live in Bogota at moderate altitude (2600 m, barometric pressure 560 mmHg, inspired oxygen pressure 28% lower than sea level). This population is composed of native (born and raised at moderate altitude) and acclimatized groups (born at lower altitudes).

Age, sex, exercise mode (cycle ergometer, treadmill), exercise protocol and training status affects measured $VO_{2\,max}$ in CPET [2]; in addition, for the same individual, $VO_{2\,max}$ and maximal work rate (WR_{max}) during cycle ergometer CPET are about 10% lower in acute moderate hypoxia than in normoxia [3].

Actual predictive equations for $VO_{2\,max}$ were developed from studies in low altitude populations [4], the accuracy of these equations in subjects permanently exposed and exercising at moderate altitude is unknown. The accuracy of $VO_{2\,max}$ predicted values for a different population should be evaluated against measured values, taking into account correlation and agreement analysis as well as by paired group comparisons.

OBJECTIVE

To determine the accuracy of published cycle ergometer equations for predicting $VO_{2\,max}$ in native and acclimatized young admixed Andean residents at moderate altitude.

METHODS

Selection of predictive maximal oxygen consumption equations

A systematic literature search in Medline® and Embase® databases identified 18 studies, all conducted at low altitude, reporting 57 predictive equations for $VO_{2\,max}$; **figure 1** summarizes inclusion criteria for retrieved studies and selection process.

Design

Secondary data analysis from "Test 2640" cross-sectional study; we included 399 healthy non-smoking, non athlete, young adults living at moderate altitude in Bogota. Subjects were assigned by sex and altitude exposure to four altitude subgroups.

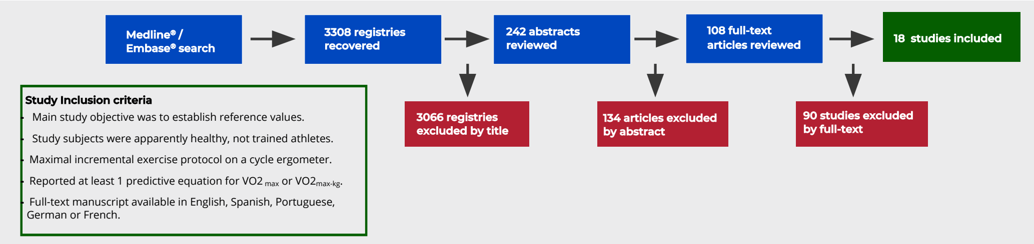
Natives: Subjects born and raised above 2500 m:

167 men, 155 women.

Acclimatized: Subjects born and raised (at least first their 14 years of life) below 500 m, but living in altitude:

39 men, 38 women.

Figure 1. Inclusion criteria for retrieved studies and selection process.



Exercise protocol

Subjects performed an incremental (ramp) maximal CPET in an electronically-braked cycle ergometer with continuous breath-by-breath gas analysis and 12-lead electrocardiography recording, earlobe capillary lactic acid concentration was sampled every 2.5 min. **Figure 2** shows subject monitoring during exercise.

Figure 2. Subject monitoring during maximal CPET.

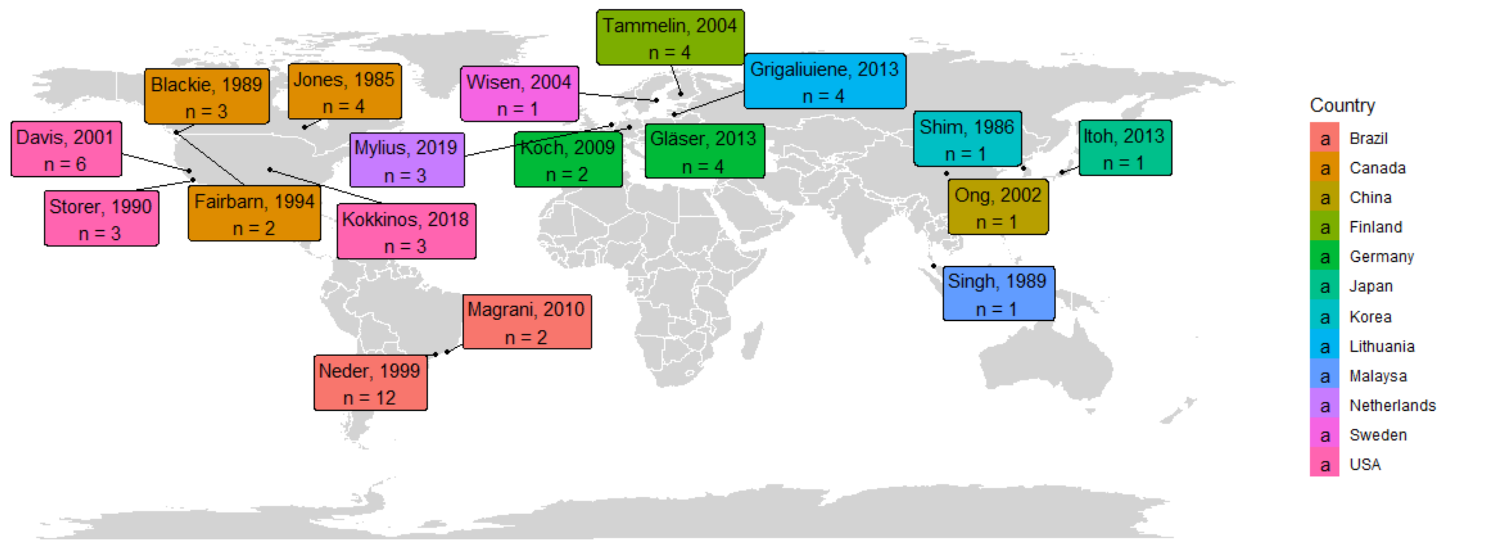
All subjects included for analysis fulfilled at least two of the fol-lowing maximal exercise criteria [5]:

- Respiratory exchange ratio (RER) > 1.1 at the end of exercise phase
- Maximal heart rate (HR_{max}) > 85% of predicted HR_{max} by Tanaka [6].
- Maximal lactate concentration (Lac_{max}) > 8 mmol/L (recovery phase).

Statistical analysis

After distribution evaluation (Shapiro-Wilks test), altitude subgroups were compared by sex for main CPET parameters (Wilcoxon rank-sum test); measured and predicted $VO_{2\,max}$ values were compared within the same altitude subgroup (Wilcoxon signed-rank test); for equations showing strong correlation with measured values (r > 0.7, Pearson's test) an agreement analysis was performed (Lin's concordance correlation test); finally, graphic Bland-Altman analysis were made for equations with strong agreement (Lin's coefficient - $\rho_c > 0.8$). Type 1 error level was pre-established at $\alpha = 0.05$ for all analysis.

Figure 3. Predictive $VO_{2\,max}$ equations on cycle ergometer by first author, year of publication and country.



RESULTS

Altitude subgroups by sex were similar in most demo-graphic, respiratory and hematologic parameters, they also were similar in Native American ancestry proportions (NAAP).

For both sexes, native subgroups had higher absolute $VO_{2\,max}$, $VO_{2\,max}$ per kilogram of body weight ($VO_{2\,max\text{-}kg}$), absolute maximal workrate (W_{max}) and W_{max} per kilogram of body weight ($W_{max\text{-}kg}$). **Table 1** summarizes the main characteristics of study subjects.

From 27 absolute $VO_{2\,max}$ equations applied for men, four predicted values similar to measured values for only one altitude subgroup with weak correlation (p > 0.05 NS, r < 0.7); three other equations overestimated predicted values with strong correlation but weak agreement in both subgroups (p < 0.05, r > 0.7, ρ_c < 0.8). **Figure 4** compares measured and predicted absolute $VO_{2\,max}$ values on cycle ergometer to seven selected men's equations by altitude subgroup.

Table 1. Main characteristics of study subjects: median (interquartile range).

	Male			Female		
	Native	Acclimatized	p value	Native	Acclimatized	p value
Demographics						
n	167	39		155	38	
Age [yr]	22.4 (3.01)	20.2 (2.84)	< 0.001	21.3 (3.18)	20.7 (3.17)	NS
Weight [kg]	63.2 (9.5)	66.1 (8.5)	NS	55.2 (7.60)	55.1 (7.42)	NS
Height [cm]	171.3 (7.10)	172 (8.69)	NS	159.5 (7.94)	158.5 (8.87)	NS
BMI (kg/m^2)	21.7 (3.08)	21.6 (2.14)	NS	21.5 (2.74)	21.3 (2.49)	NS
Body fat (%)	13.1 (5.55)	12.7 (3.55)	NS	23.5 (6.2)	23.0 (5.87)	NS
Pulmonary function						
FEV1 [L]	4.37 (0.69)	4.25 (0.75)	NS	3.24 (0.56)	3.2 (0.60)	NS
FVC [L]	5.09 (0.8)	4.93 (1.06)	NS	3.77 (0.63)	3.49 (0.74)	< 0.05
FEV/FVC	0.84 (0.08)	0.87 (0.08)	NS	0.87 (0.07)	0.90 (0.07)	< 0.01
MVV [L]	192. (39.8)	187. (38.2)	NS	130. (25.3)	135. (18.3)	NS
Blood markers						
Hb [g/dL]	16.6 (0.95)	16.9 (1.09)	NS	14.7 (1.1)	14.7 (0.95)	NS
EAP (%)	49.9 (18.1)	43.7 (18.4)	< 0.01	50.9 (23.7)	49.9 (16.4)	NS
AAP (%)	9.95 (8.65)	13.3 (10.6)	< 0.05	10.3 (7.4)	13.2 (12)	NS
NAAP (%)	38.1 (19.8)	38.9 (16)	NS	37.7 (20.5)	33.2 (18.5)	NS
Exercise parameters						
$VO2_{max}$ [mL/min]	2914.7 (652.2)	2599.1 (626.8)	< 0.001	1943.7 (446.4)	1723.5 (315.0)	< 0.001
$VO2_{max-kg}$ [mL/min/kg]	46.1 (9.7)	38.6 (9.4)	< 0.001	34.8 (6.5)	32.4 (5.4)	< 0.001
W_{max} [W]	272 (63.5)	234 (76.5)	< 0.001	165 (39.5)	147.5 (25.2)	< 0.01
W_{max-kg} [W/kg]	4.3 (1.0)	3.6 (0.9)	< 0.001	2.9 (0.7)	2.7 (0.4)	< 0.01
HR_{max} [beats/min]	190 (9)	196 (10)	NS	190 (12)	193 (11.25)	NS
HR_{pred} [%]	99.4 (5.6)	100. (6.1)	NS	98.4 (6.2)	99.6 (5.1)	NS
RER_{max}	1.21 (0.08)	1.22 (0.09)	NS	1.17 (0.08)	1.18 (0.08)	NS
La_{max} [mmol/L]	13.4 (3.0)	13.7 (3.7)	NS	10.9 (2.5)	10.3 (1.5)	< 0.05

From 27 absolute $VO_{2\,max}$ equations applied for women, ten predicted values similar to measured values for only one altitude subgroup with weak correlation (p > 0.05 NS, r < 0.7); two other equations overestimated predicted values with strong correlation in both subgroups and strong agreement in most subgroups (p < 0.05, r > 0.7, ρ_c > 0.8), Bland-Altman analysis showed high dispersion around the mean difference for both equations (+/- 500 mL). One additional equation underestimated predicted values with strong correlation but weak agreement in both subgroups (p < 0.05, r > 0.7, ρ_c < 0.8). **Figure 5** compares measured and predicted absolute $VO_{2\,max}$ values on cycle ergometer for 13 selected women's equations by altitude subgroup.

Figure 4. Absolute $VO_{2\,max}$, measured vs. predicted, men.

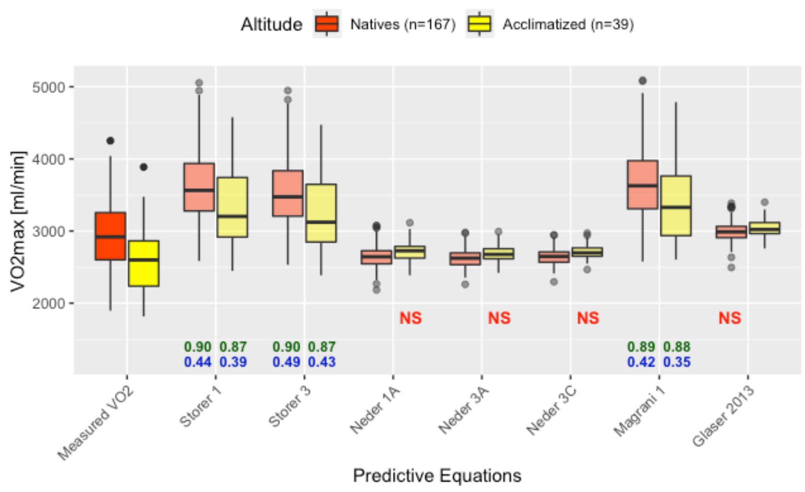
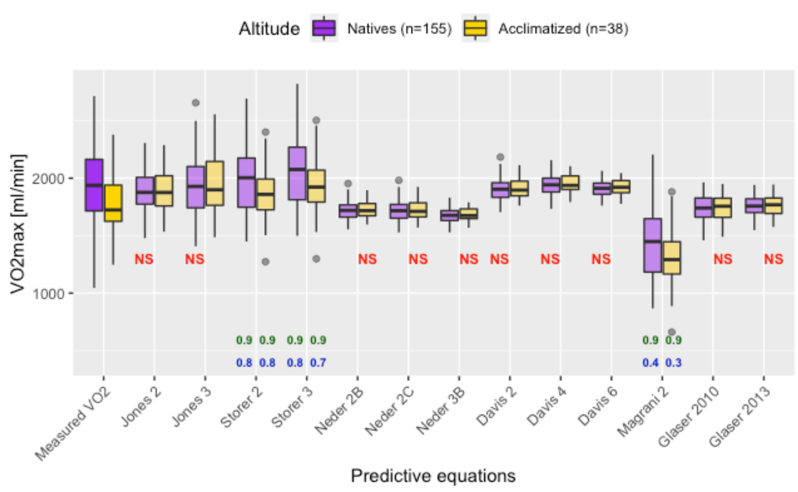


Figure 5. Absolute $VO_{2\,max}$, measured vs. predicted, women.



Measured values by altitude subgroup (darker color) compared with predicted values of the respective altitude subgroup (lighter colors), predicted values with non-significant difrerence in red (NS, p > 0.05); correlation coefficients (r) in green; concordance correlation coefficients (ρ_c) in blue.

From nine $VO_{2\,max\text{-}kg}$ equations applied for men, two predicted values similar to measured values for acclimatized subgroups only, with strong correlation but weak agreement (p > 0.05 NS, r > 0.7, ρ_c < 0.8). **Figure 6** compares measured and predicted absolute $VO_{2\,max\text{-}kg}$ values on cycle ergometer for two selected men's equations by altitude subgroup.

From seven $VO_{2\,max\text{-}kg}$ equations applied for women, one equation predicted similar values to measured values for the native subgroup only, with strong correlation and strong agreement (p > 0.05 NS, r > 0.7, ρ_c > 0.8), Bland-Altman analysis showed high dispersion around mean difference (+/- 6 mL/min/kg). **Figure 7** compares measured and predicted absolute $VO_{2\,max\text{-}kg}$ values on cycle ergometer for two selected women's equations by altitude subgroup.

Figure 6. $VO2_{max\text{-}kg}$, measured vs. predicted, men.

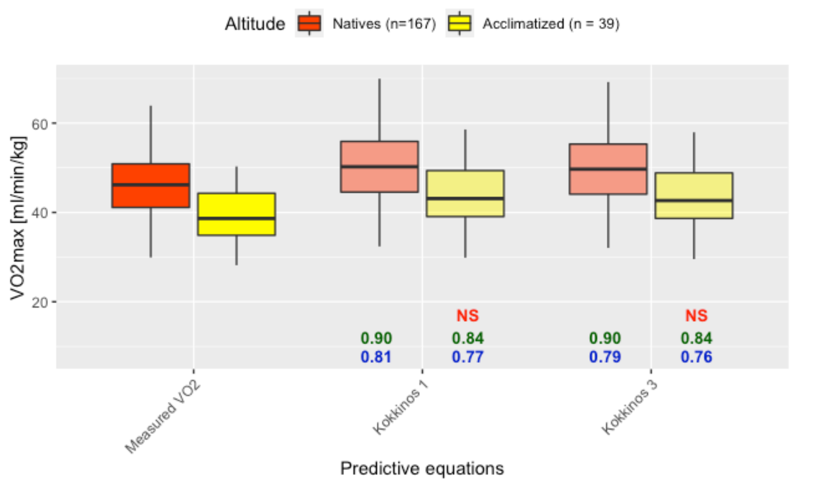
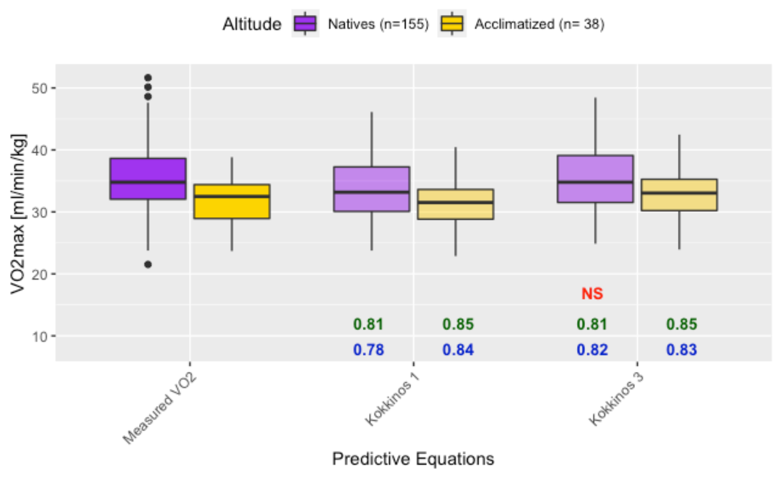


Figure 7. $VO2_{max\text{-}kg}$, measured vs. predicted, women.



Measured values by altitude subgroup (darker color) compared with predicted values of the respective altitud subgroup (ligther colors), predicted values with non-significant difrerence in red (NS, p > 0.05); correlation coefficients (r) in green; concordance correlation coefficients (ρ_c) in blue.

Figures 8 and **9** display correlation and Bland-Altman analysis in native women for Kokkinos 3 cycle ergometer $VO_{2\,max\text{-}kg}$ equation.

Figure 8. Correlation analysis for Kokkinos equation 3, native women (n=155), r = 0.81, 95% CI: 0.75 - 0.86, p < 0.05.

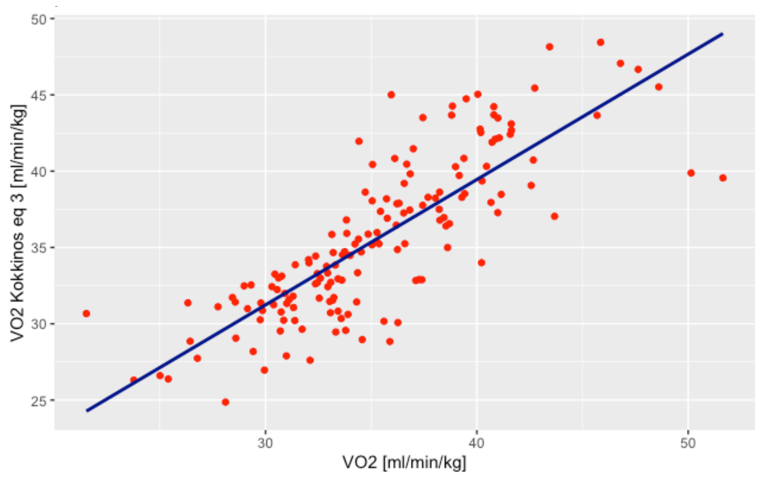
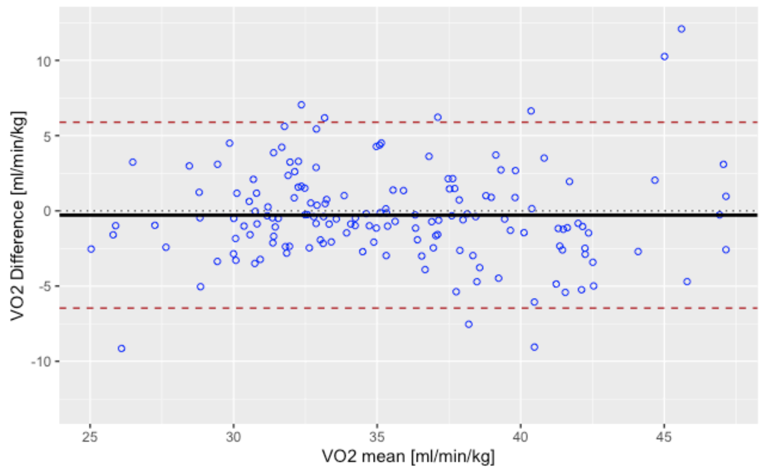


Figure 9. Bland-Altman analysis for Kokkinos equation 3, native women (n=155).



More importantly, for both man and women groups in both altitude subgroups, only those equations that included W_{max} were highly correlated (r > 0.8) with absolute $VO_{2\,max}$ or $VO_{2\,max\text{-}kg}$ measured values.

CONCLUSIONS

Available cycle ergometer predictive equations from studies carried out in low altitude populations are not accurate for predicting $VO_{2\,max}$ in healthy young admixed Andean population living at moderate altitude (native or acclimatized).

Besides hypobaric hypoxia exposure, anthropometric and lifestyle differences between high and low altitude populations should also be considered to explain this results.

Study designs for developing cycle ergometer predictive $VO_{2\,max}$ equations in moderate altitude Andean residents should take into account the degree of altitude acclimatization and should include maximal work rate as one of the equation's key variables.

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