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ARE METABOLIC EQUIVALENTS (METS) AN ACCURATE METHOD FOR ESTIMATING CHANGE IN PEAK OXYGEN CONSUMPTION AFTER CARDIAC REHABILITATION?

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Introduction

Personalised cardiac rehabilitation (CR) exercise prescriptions should be based on an individualised assessment that includes determination of patients' cardiorespiratory fitness (CRF) [ACPICR, 2015]. Maximal cardiopulmonary exercise testing (CPET) is the "gold standard" method for determining CRF (Mezzani et al. 2013). However, CPET is not widely available in the UK and estimates of VO_{2peak} are typically used.

Calculation of peak metabolic equivalents (METs) derived from workloads achieved during incremental exercise testing is a common approach to estimating VO_{2peak}, a marker of CRF (ACSM, 2013; Buckley, et al. 2016). One MET is assumed to equate to a resting VO_2 of 3.5 $ml{\cdot}kg^{-1}{\cdot}min^{-1}$ (Wasserman, *et al.* 2011). Increases in functional capacity reported from sequential exercise tests may be expressed in METs. Peak estimated METs achieved during maximal exercise testing in turn, can be used to quantify changes in CRF following exercise interventions (ACSM, 2013; ACPICR, 2015).

Large discrepancies between estimated (METs), and directly determined VO_{2peak} have previously been reported (Froelicher et al. 1984; Kavanagh et al. 2002). Peak estimated METs may therefore, not accurately estimate VO_{2peak} change following CR. Previous investigators have found no correlation (r=0.24; p=0.100) between VO_{2peak} change and peak estimated MET change in 50 patients with coronary heart disease [CHD] (Milani et al. 1995). Stuto et al. (2013) also present data indicating that the increase in directly determined VO_{2peak} following CR was approximately half (14.7%) of the 28.8% increase in estimated peak METs following CR amongst 180 CHD patients.

This study therefore investigated the accuracy of estimating changes in VO_{2peak} in patients with CHD, by comparing patients' directly determined VO_{2peak} to VO_{2peak} estimated through the American College of Sports Medicine leg cycling equation (ACSM, 2013).

Methods

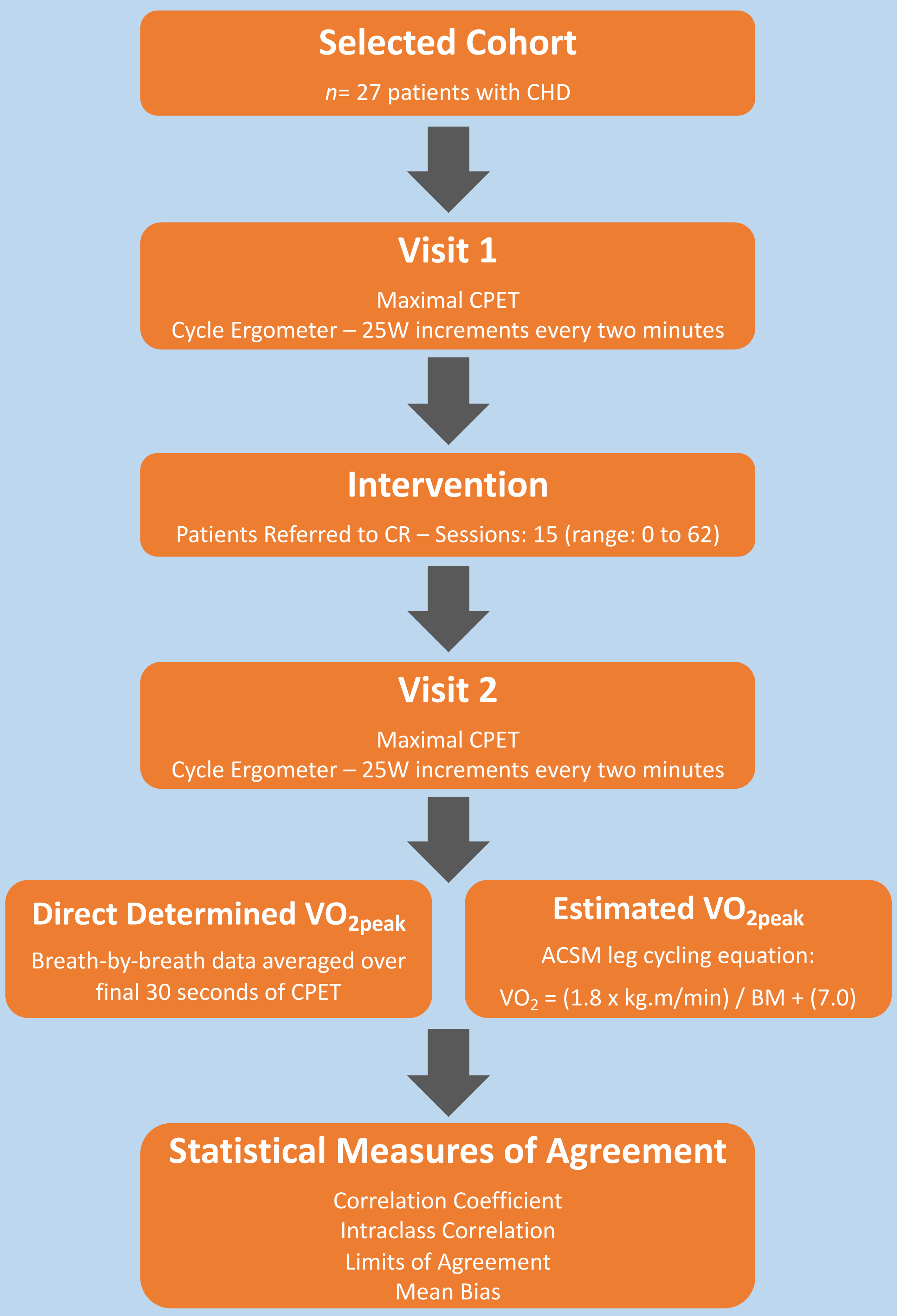

Figure 1 - Key experimental stages of the study

CHD = Coronary Heart Disease; CPET = Cardiopulmonary Exercise Testing; CR = Cardiac Rehabilitation; BM = Body Mass

Figure 1 shows the key stages involved in patient assessment, testing and, the statistical process applied to determine agreement between estimated VO_{2peak} and directly determined VO_{2peak}. All patients underwent maximal CPET, before and after referral to a CR exercise regime. Directly determined VO_{2peak} was calculated by averaging breath-by-breath metabolic gas exchange data over the final 30 seconds of CPET. Estimated VO_2 was determined using the ACSM (2013) leg cycle equation. Correlation coefficients, intraclass correlations (ICC), Bland-Altman plots (with limits of agreement (LoA)) were used to determine agreement between changes in directly determined VO_{2peak} and changes in estimated VO_{2peak}.

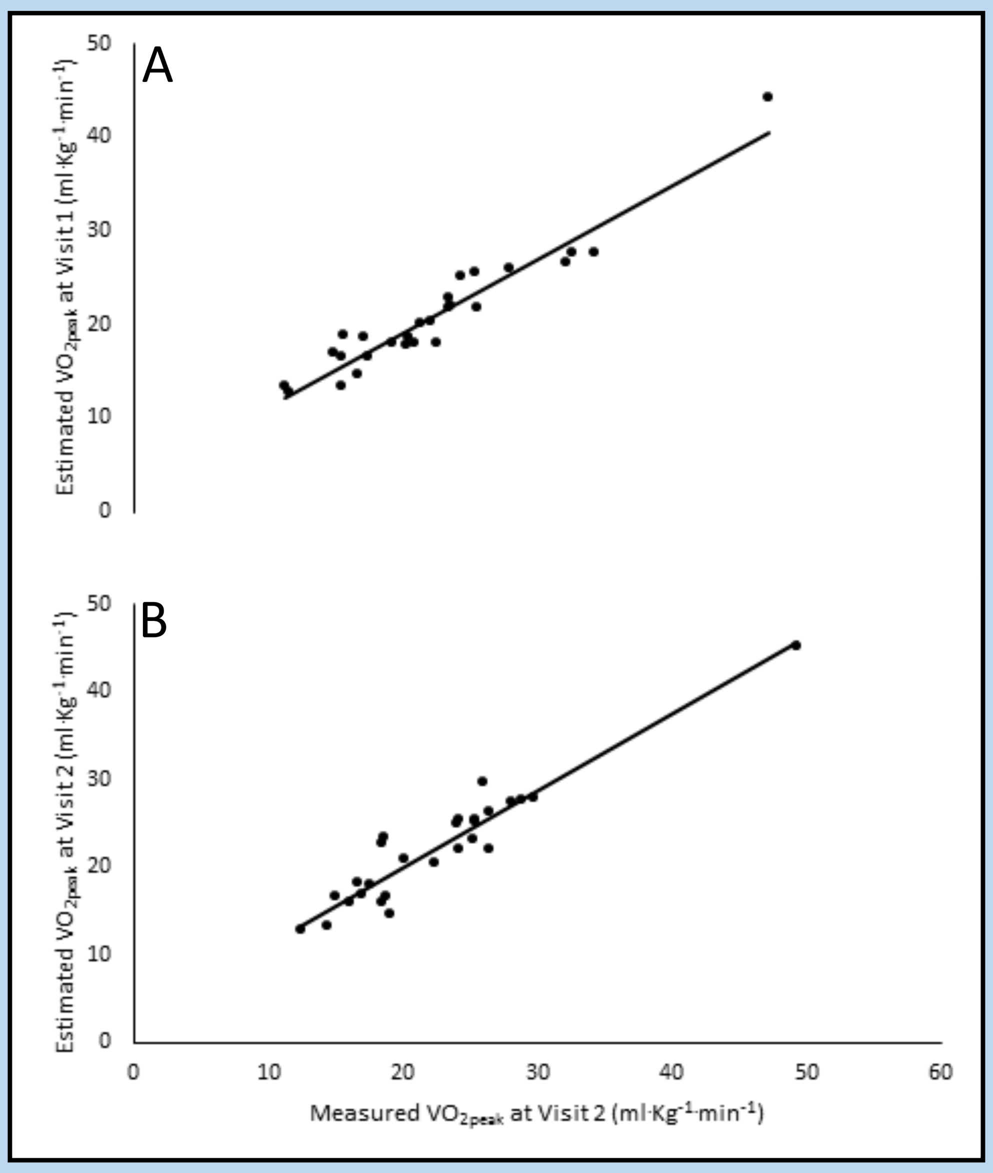

Figure 2 – Linear regression showing the relationship between directly determined VO_{2peak} and estimated VO_{2peak} for visit 1 (panel A; r =0.958, p<0.001) and visit 2 (panel B; r=0.945, p<0.001)

VO_{2peak} = peak oxygen uptake

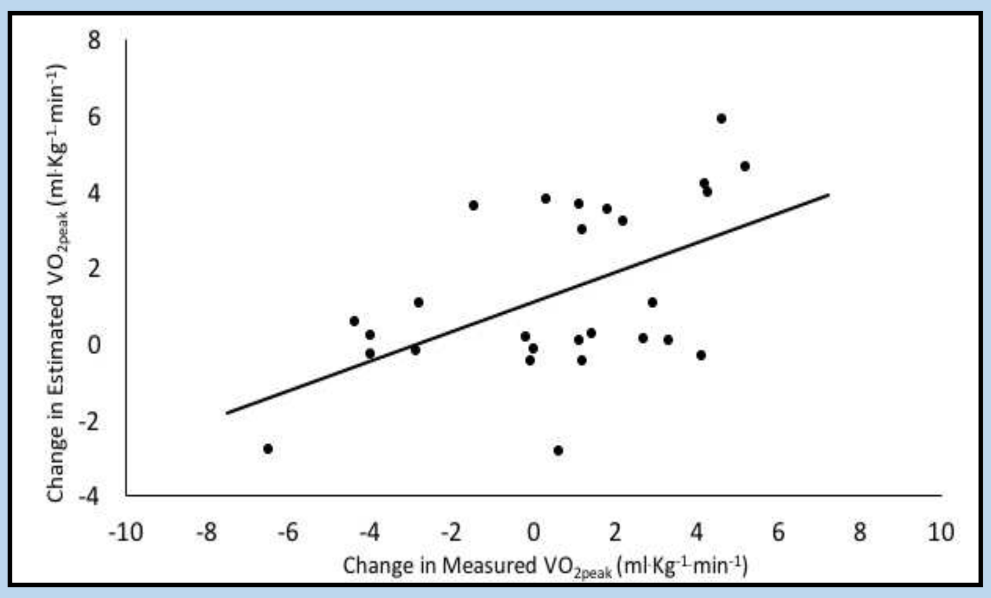

Figure 3 – Linear regression between directly determined VO_{2peak} change and estimated VO_{2peak} change between visit 1 and 2 (r=0.527, p<0.05).

VO_{2peak} = peak oxygen uptake

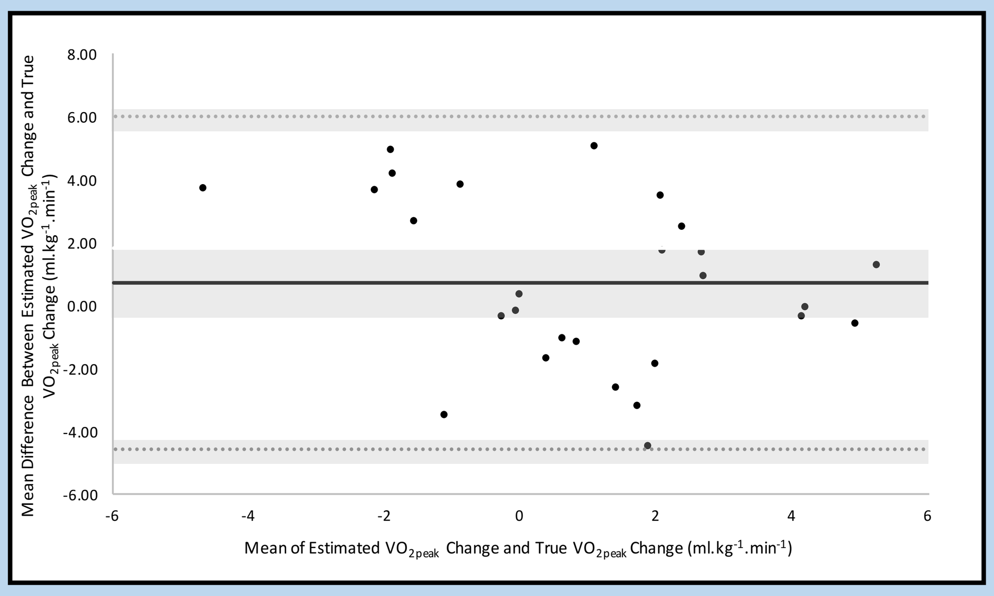

Figure 4 – Bland-Altman plot showing mean bias (0.7 $ml{\cdot}kg^{-1}{\cdot}min^{-1}$), LoA (-4.6.3 to 5.9 $ml{\cdot}kg^{-1}{\cdot}min^{-1}$) with 95% CI (grey shaded area) between directly determined and estimated VO_{2peak}.

LoA = Limits of Agreement

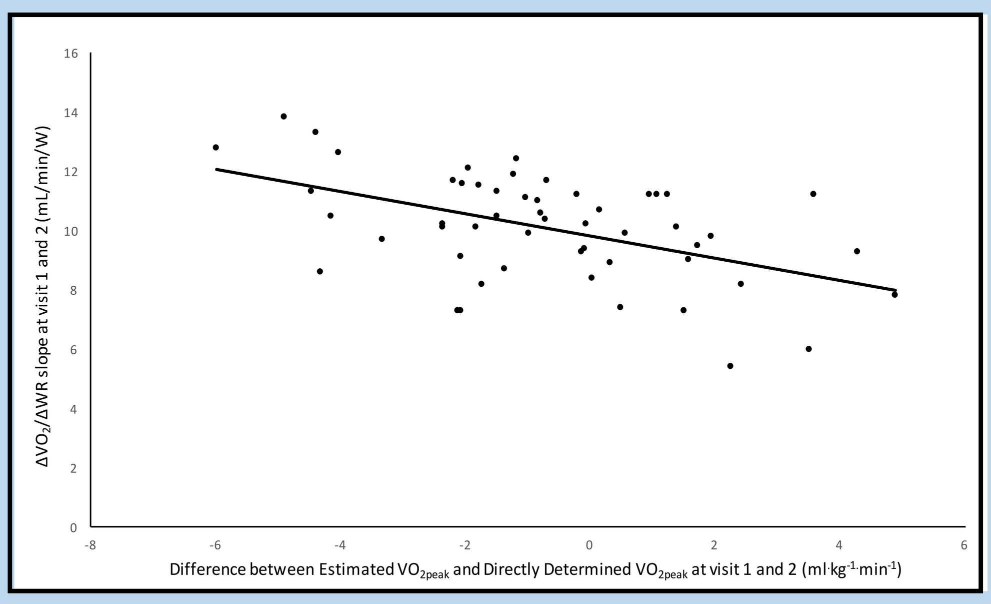

Figure 5 – Linear regression showing a significant, moderate negative correlation between $\Delta VO_2/\Delta WR$ slope and estimated VO_{2peak} measurement error.

VO_{2peak} = peak oxygen uptake; $\Delta VO_2/\Delta WR$ = change in VO_2 as a function of change in work rate

Results

27 patients (88.9% male; 59.5 ± 10.0 years; body mass index 29.6 $kg{\cdot}m^{-2}$) with CHD were recruited. Mean left ventricular ejection fraction was 58.9 ± 9.2%. Resting systolic, and diastolic blood pressure were 140 ± 19 and 83 ± 10mmHg, respectively. Resting heart rate was 60 ± 7bpm. The majority of patients were referred to CR having sustained a myocardial infarction (59.3%), 37% of patients had been referred after elective percutaneous coronary intervention. Only one patient (3.7%) was referred having undergone coronary artery bypass grafting.

Changes in CRF are shown in Table 1. Despite an increase in work rate and exercise time, VO_{2peak} did not increase significantly (0.5 $ml{\cdot}kg^{-1}{\cdot}min^{-1}$; 95% CI -0.6 to 1.8 $ml{\cdot}kg^{-1}{\cdot}min^{-1}$) following CR. Consistent with the increased work rate, there was a significant increase in peak estimated METs (0.4 METs; 95% CI 0.1 to 0.6 METs). This corresponded to an estimated VO_{2peak} increase of 1.4 $ml{\cdot}kg^{-1}{\cdot}min^{-1}$. The mean $\Delta VO_2/\Delta WR$ slopes (measure of aerobic efficiency) was within normal limits (>8.4 ml/min/W), however 19% of all exercise tests had abnormal $\Delta VO_2/\Delta WR$ slopes.

Table 1 – Cardiorespiratory Fitness Change

Variable	Visit 1 (±SD)	Visit 2 (±SD)	Mean Change (95% CI)	P-Value
VO_{2peak} ($ml{\cdot}kg^{-1}{\cdot}min^{-1}$)	21.9 ± 7.6	22.5 ± 7.2	0.5 (-0.6 to 1.8)	0.332
Estimated VO_{2peak} ($ml{\cdot}kg^{-1}{\cdot}min^{-1}$)	20.9 ± 6.4	22.2 ± 6.7	1.3 (0.4 to 2.2)	0.006*
Estimated peak METs	6.0 ± 1.8	6.4 ± 1.9	0.4 (0.1 to 0.6)	0.006*
Exercise Test Duration (Sec)	585.4 ± 228.1	651.8 ± 250.0	66.4 (9.9 to 122.9)	0.023*
Peak Watts	111.1 ± 49.2	118.5 ± 48.8	7.4 (1.4 to 13.4)	0.018*
$\Delta VO_2/\Delta WR$ slope	10.2 ± 2.0	10.2 ± 2.1	0.1 (-0.7 to 0.9)	0.829

VO_{2peak} = Peak Oxygen Uptake; METs = Metabolic Equivalents; Sec=seconds; $\Delta VO_2/\Delta WR$ slope = Change in Oxygen Uptake Vs. Change in Work Rate slope

*= statistically significant

Measures of agreement for CPET variables are presented in Table 2. There was a significant association between directly determined VO_{2peak} and estimated VO_{2peak} on both pre and post- cardiac rehabilitation visits (Figure 2A and 2B). Of note, was the correlation between changes in directly-determined VO_{2peak} and estimated VO_{2peak} (Figure 3; r=0.527, p=0.05). The ICC between the two measurements was not significant (ICC 0.358; 95% CI -0.442 to 0.711; p=0.138). Bland-Altman analysis (Figure 4) showed the mean bias for changes in VO_{2peak} to be 0.7 $ml{\cdot}kg^{-1}{\cdot}min^{-1}$ (95% CI -0.4 to 1.8 $ml{\cdot}kg^{-1}{\cdot}min^{-1}$; p=0.178). The LoA were -4.7 to 5.9 $ml{\cdot}kg^{-1}{\cdot}min^{-1}$ (lower LoA 95% CI: -5.1 to -4.3; upper LoA 95% CI: 5.5 to 6.3 $ml{\cdot}kg^{-1}{\cdot}min^{-1}$). There was a significant, moderate negative correlation between VO_{2peak} measurement error (estimated VO_{2peak} minus directly determined VO_{2peak}) and $\Delta VO_2/\Delta WR$ slope (Figure 5, r=-0.496, p<0.001).

Table 2 – Measures of Agreement between Measured and Estimated VO_{2peak}

	Correlation (r)	Mean Bias ($ml{\cdot}kg^{-1}{\cdot}min^{-1}$)	LoA ($ml{\cdot}kg^{-1}{\cdot}min^{-1}$)	ICC (95% CI)
VO_{2peak} Vs. Estimated VO_{2peak} at Visit 1	0.958*	-1.0*	-5.6 to 3.6	0.967 (0.921 to 0.986)*
VO_{2peak} Vs. Estimated VO_{2peak} at Visit 2	0.945*	0.3	-4.8 to 4.3	0.971 (0.936 to 0.987)*
Change in Estimated VO_{2peak} Vs. Measured VO_{2peak}	0.527*	0.7	-4.6 to 5.9	0.358 (-0.442 to 0.711)

LoA = Limits of Agreement; ICC = Intraclass Correlation; VO_{2peak} = Peak Oxygen Uptake

*= Statistically Significant

Conclusion

Estimated METS showed a high correlation with directly-measured VO_{2peak} in a representative cohort of patients attending CR. However, the estimated MET changes observed following CR correlated less well with direct measures and showed poor measurement agreement. Estimated METs may not accurately reflect mean VO_{2peak} changes following a CR exercise training intervention.

Our findings may in part, be due to poor aerobic efficiency. We found that $\Delta VO_2/\Delta WR$ slope was negatively correlated with estimated VO_{2peak} measurement error (r=-0.496, p<0.001) indicating that estimates of VO_{2peak} over-predict directly determined VO_{2peak} when patients are aerobically 'inefficient'. Inefficient cardiometabolic responses to exercise such as delayed oxygen kinetics, may prolong dependence on anaerobic metabolism (Mezzani et al. 2009) during sequential work rate transitions. In such instances, the assumptions of linearity between work rate and VO_2 would not apply and work rate would not be indicative of VO_2. Accurately predicting VO_{2peak} changes in CHD patients, as evidenced by our findings and others (Froelicher et al. 1984; Milani et al. 1995; Stuto et al. 2013), poses significant challenges, particularly at an individual patient level.

Increasing VO_{2peak} through structured exercise training improves survival (Vanhees et al. 1995) in patients with CHD and, consequently, improving VO_{2peak} remains a key objective for CR practitioners. Practitioners need to have confidence in their outcome measures. Given that CR programme outcome data are often expressed as estimated METs, there is a requirement to examine the suitability of METs to estimate directly-determined changes in VO_{2peak}.

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