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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

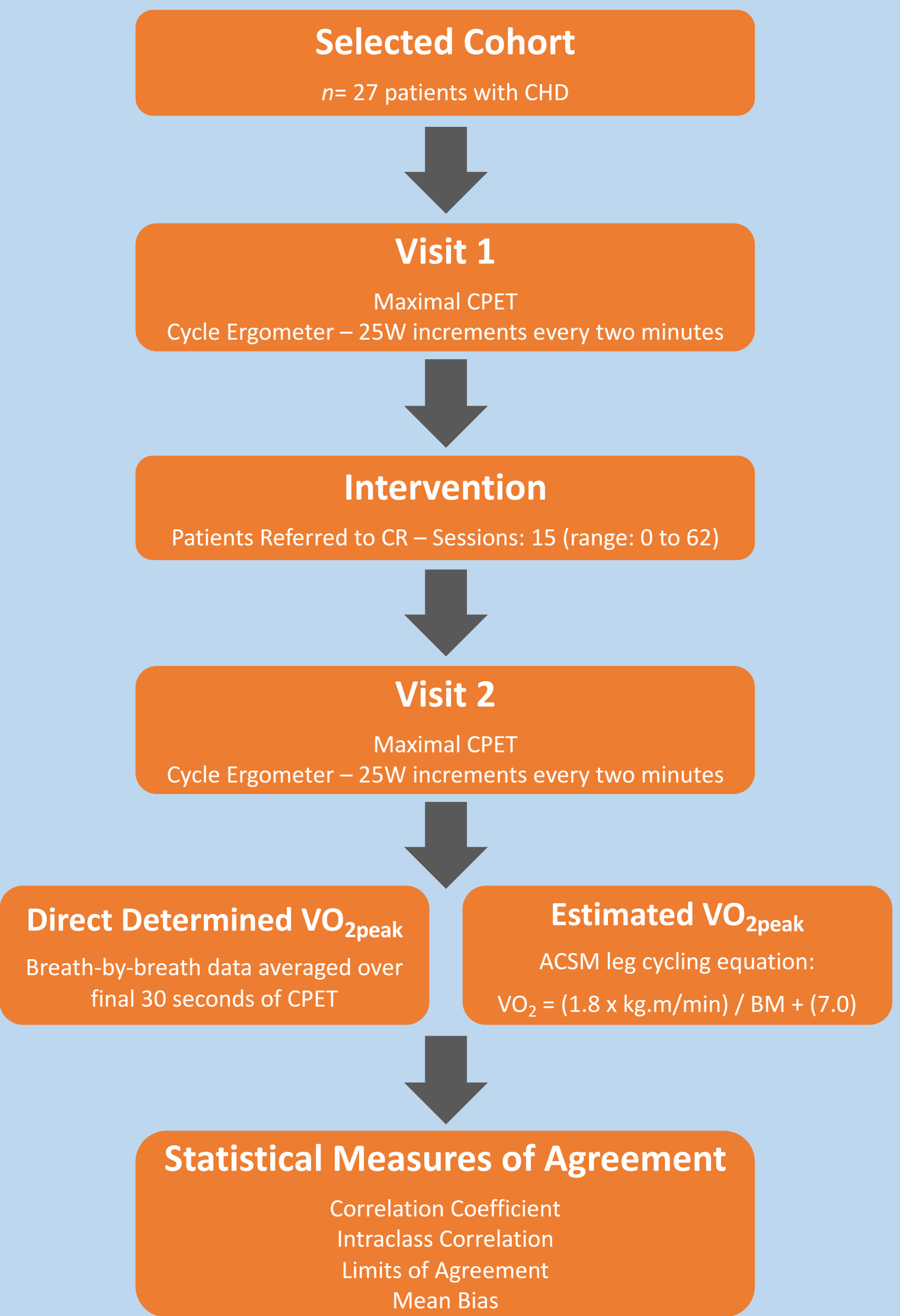
Personalised cardiac rehabilitation (CR) exercise prescriptions should be based on an individualised assessment that includes determination of patients' cardiorespiratory fitness (CRF) [ACPICR, 2015]. Maximal cardiopulmonary exercise testing (CPET) is the "gold standard" method for determining CRF (Mezzani 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  $3.5 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$  (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 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).

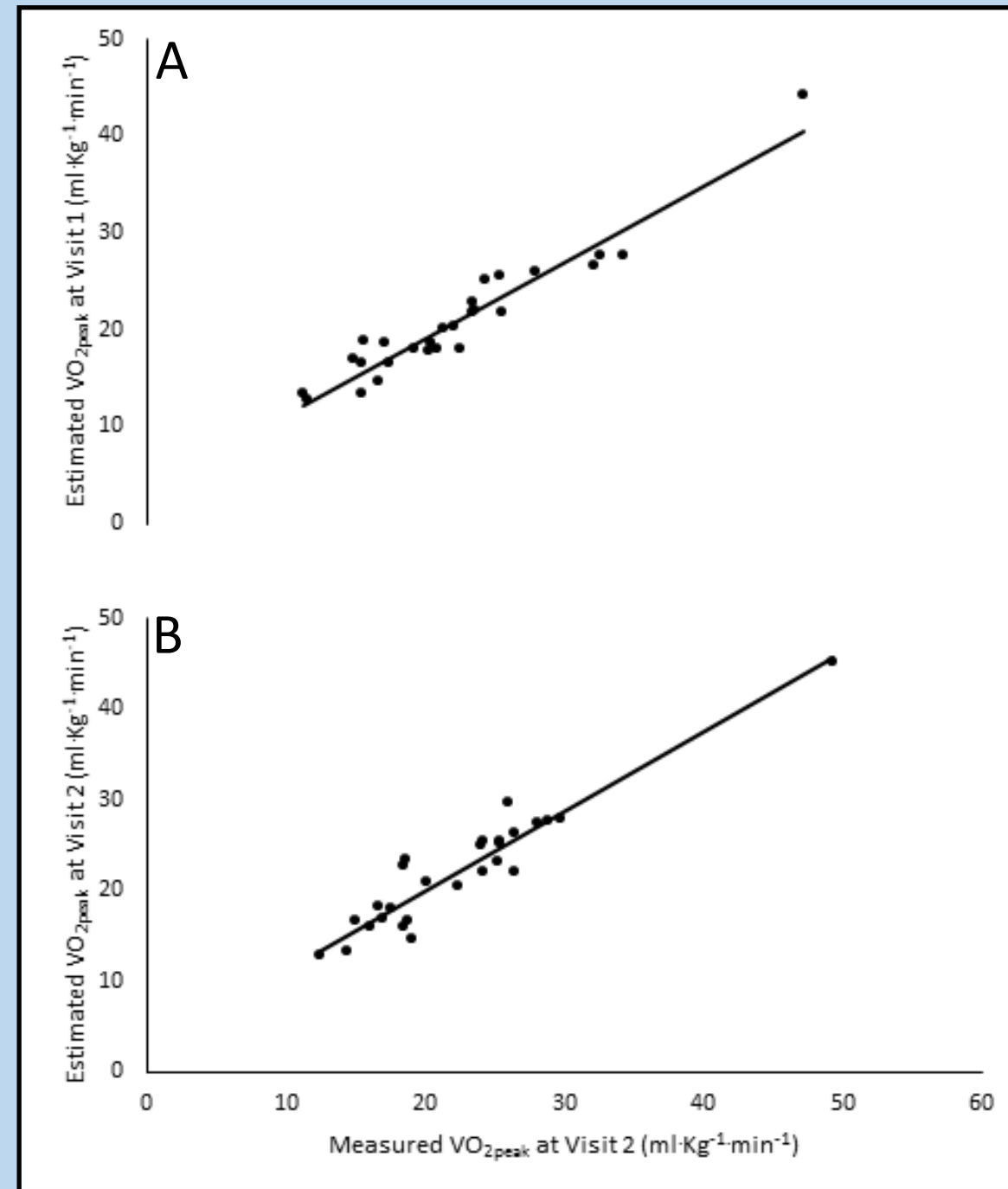
## Methods



**Figure 1** - Key experimental stages of the study

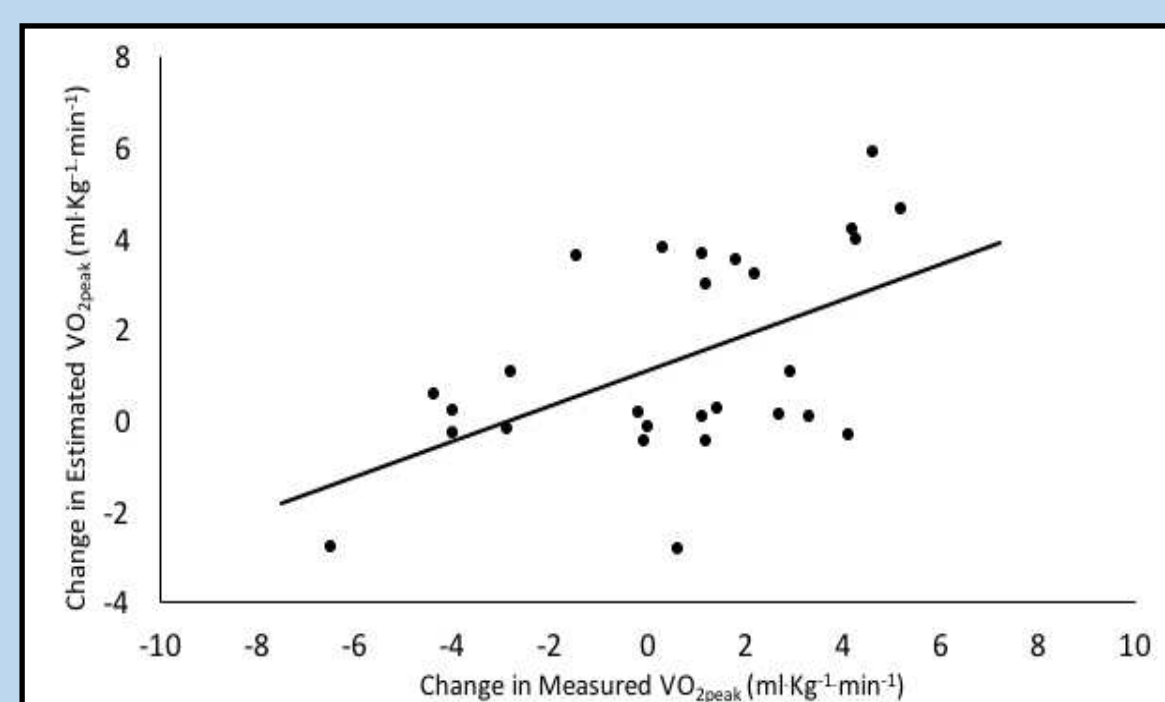
CHD = Coronary Heart Disease; CPET = Cardiopulmonary Exercise Testing; CR = Cardiac Rehabilitation; BM = Body Mass

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  $VO_{2peak}$ .



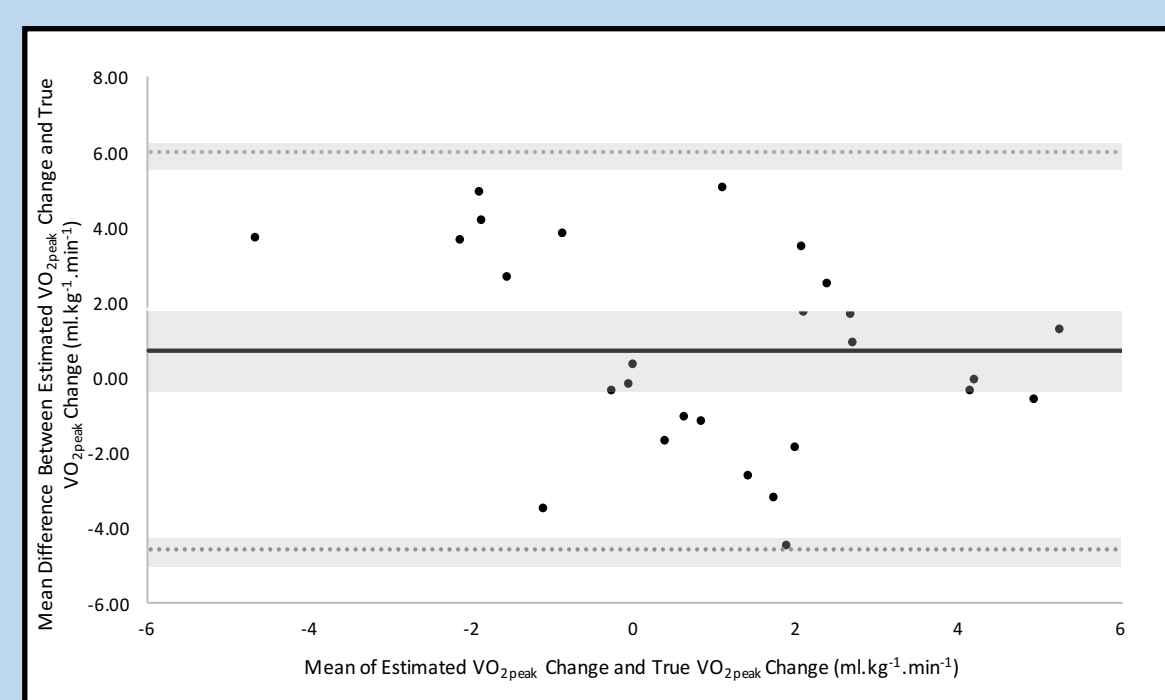
**Figure 2** – Linear regression showing the relationship between directly determined  $VO_{2peak}$  and estimated  $VO_{2peak}$  for visit 1 (panel A;  $r=0.958$ ,  $p<0.001$ ) and visit 2 (panel B;  $r=0.945$ ,  $p<0.001$ )

$VO_{2peak}$  = peak oxygen uptake



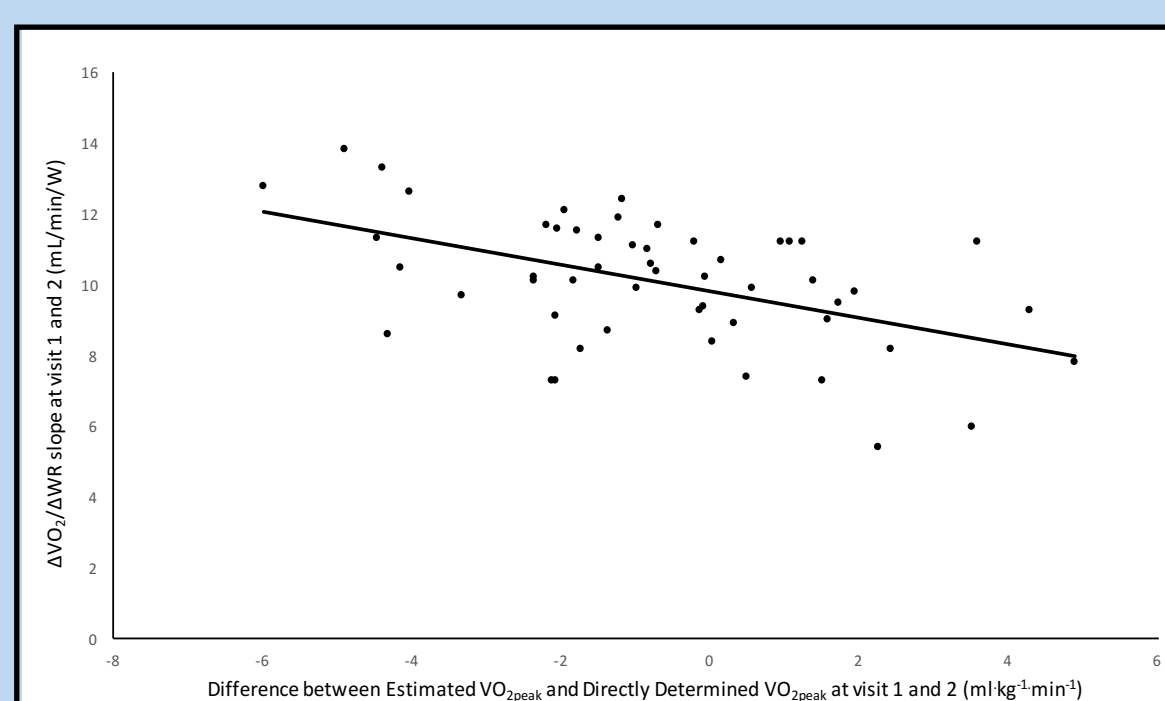
**Figure 3** – Linear regression between directly determined  $VO_{2peak}$  change and estimated  $VO_{2peak}$  change between visit 1 and 2 ( $r=0.527$ ,  $p<0.05$ ).

$VO_{2peak}$  = peak oxygen uptake



**Figure 4** – Bland-Altman plot showing mean bias ( $0.7 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ), LoA ( $-4.63$  to  $5.9 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ) 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;  $59.5 \pm 10.0$  years; body mass index  $29.6 \text{ kg}\cdot\text{m}^{-2}$ ) with CHD were recruited. Mean left ventricular ejection fraction was  $58.9 \pm 9.2\%$ . Resting systolic, and diastolic blood pressure were  $140 \pm 19$  and  $83 \pm 10 \text{ mmHg}$ , respectively. Resting heart rate was  $60 \pm 7 \text{ bpm}$ . 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 ( $0.5 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ; 95% CI  $-0.6$  to  $1.8 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ) following CR. Consistent with the increased work rate, there was a significant increase in peak estimated METs ( $0.4 \text{ METs}$ ; 95% CI  $0.1$  to  $0.6 \text{ METs}$ ). This corresponded to an estimated  $VO_{2peak}$  increase of  $1.4 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ . The mean  $\Delta VO_2/\Delta WR$  slopes (measure of aerobic efficiency) was within normal limits ( $>8.4 \text{ ml}/\text{min}/\text{W}$ ), however 19% of all exercise tests had abnormal  $\Delta VO_2/\Delta WR$  slopes.

**Table 1** – Cardiorespiratory Fitness Change

Variable	Visit 1 ( $\pm$ SD)	Visit 2 ( $\pm$ SD)	Mean Change (95% CI)	P-Value
$VO_{2peak}$ ( $\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ )	$21.9 \pm 7.6$	$22.5 \pm 7.2$	$0.5 (-0.6 \text{ to } 1.8)$	0.332
Estimated $VO_{2peak}$ ( $\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ )	$20.9 \pm 6.4$	$22.2 \pm 6.7$	$1.3 (0.4 \text{ to } 2.2)$	0.006*
Estimated peak METs	$6.0 \pm 1.8$	$6.4 \pm 1.9$	$0.4 (0.1 \text{ to } 0.6)$	0.006*
Exercise Test Duration (Sec)	$585.4 \pm 228.1$	$651.8 \pm 250.0$	$66.4 (9.9 \text{ to } 122.9)$	0.023*
Peak Watts	$111.1 \pm 49.2$	$118.5 \pm 48.8$	$7.4 (1.4 \text{ to } 13.4)$	0.018*
$\Delta VO_2/\Delta WR$ slope	$10.2 \pm 2.0$	$10.2 \pm 2.1$	$0.1 (-0.7 \text{ to } 0.9)$	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  $0.7 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$  (95% CI  $-0.4$  to  $1.8 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ;  $p=0.178$ ). The LoA were  $-4.7$  to  $5.9 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$  (lower LoA 95% CI:  $-5.1$  to  $-4.3$ ; upper LoA 95% CI:  $5.5$  to  $6.3 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ). 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 ( $\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ )	LoA ( $\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ )	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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