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ORIGINAL ARTICLE

The morphology and stability of the oxygen pulse curve during cardiopulmonary exercise testing

Morphologie et stabilité de la courbe du pouls d'oxygène lors d'une épreuve d'exercice cardiopulmonaire

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Oxygen pulse ;
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Reliability ;
Agreement

Summary
Objectives. — This study aimed to assess the relative and absolute reliability (agreement) of various parameters derived from the oxygen pulse ($\dot{O}_2$*Pulse*) curve during cardiopulmonary exercise testing (CPET), a tool critical for evaluating cardiopulmonary function and fitness.
Design. — Retrospective test-retest reliability study.
Equipment and methods. — Twelve recreationally active male participants underwent two CPETs within a test-retest interval of $\leq$ 72 hours. The study analysed different components of the $\dot{O}_2$*Pulse* curve, including the area under the curve (AUC) and its slope in relation to the work-rate. Statistical analysis was then undertaken to determine the associated intraclass correlation coefficient (reliability), standard error of measure and minimal detectable change (agreement — SEM and MDC) values.
Results. — Statistical analysis indicated a range in the reliability of $\dot{O}_2$*Pulse* curve parameters, from poor (intraclass correlation coefficient, ICC = 0.49) for slope values to excellent (ICC = 1.00) for the filtered $\dot{O}_2$*Pulse* AUC. The mean percentage minimal detectable change (%MDC) for filtered AUC was calculated at 15 $\pm$ 0.8, signifying the threshold for confidently determining true change.

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Conclusion. — The findings suggest that the $\dot{O}_2Pulse$ curve is a stable and robust variable in CPET, offering significant insights into cardiovascular health. These results have implications for exercise prescription, risk stratification, and rehabilitation in clinical settings. The study highlights the importance of adopting consistent reporting criteria like %MDC in future studies for better comparison across research and clinical practices.

MOTS CLÉS
Pouls d'oxygène ;
Épreuve d'exercice cardiopulmonaire ;
Fiabilité ;
Accord

Résumé
Objectifs. — Cette étude visait à évaluer la fiabilité relative et absolue (accord) de divers paramètres dérivés de la courbe du pouls d'oxygène ($\dot{O}_2Pulse$) lors de l'épreuve d'exercice cardiopulmonaire (CPET), un outil essentiel pour évaluer la fonction et la condition cardiopulmonaires.
Conception. — Étude rétrospective de fiabilité test-retest.
Équipement et méthodes. — Douze participants masculins, actifs de manière récréative, ont subi deux CPETs dans un intervalle de test-retest de $\leq$ 72 heures. L'étude a analysé différents composants de la courbe $\dot{O}_2Pulse$, y compris l'aire sous la courbe (AUC) et sa pente en relation avec le taux de travail. Une analyse statistique a ensuite été réalisée pour déterminer le coefficient de corrélation intraclasse associé (fiabilité), l'erreur standard de mesure et les valeurs de changement minimal détectable (accord — SEM et MDC).
Résultats. — L'analyse statistique a indiqué une variation de la fiabilité des paramètres de la courbe $\dot{O}_2Pulse$, allant de faible (coefficient de corrélation intraclasse, ICC = 0,49) pour les valeurs de pente à excellente (ICC = 1,00) pour l'AUC $\dot{O}_2Pulse$ filtrée. Le pourcentage moyen de changement minimal détectable (% MDC) pour l'AUC filtrée a été calculé à $15 \pm 0{,}8$, signifiant le seuil pour déterminer avec confiance un véritable changement.
Conclusion. — Les résultats suggèrent que la courbe $\dot{O}_2Pulse$ est une variable stable et robuste en CPET offrant des informations significatives sur la santé cardiovasculaire. Ces résultats ont des implications pour la prescription d'exercice, la stratification des risques et la réhabilitation dans les milieux cliniques. L'étude souligne l'importance d'adopter des critères de rapport cohérents comme le % MDC dans les études futures pour une meilleure comparaison entre la recherche et les pratiques cliniques.

1. Introduction

Cardiopulmonary exercise testing (CPET) allows clinicians to non-invasively interrogate the function and capacity of the cardiopulmonary system during maximal, or symptom limited graded exercise [1]. CPET permits the simultaneous collection of multiple variables, such as minute ventilation (VE), oxygen uptake ($\dot{V}O_2$) and carbon dioxide production ($\dot{V}CO_2$). The data gathered during CPET is used in a variety of settings, from prescribing and guiding exercise intensity, to identifying potential disease pathology and determining a patient's readiness for surgery [2].

As with many physiological examinations, the test-retest reliability of CPET (cardiopulmonary exercise testing) is influenced by a variety of intrinsic (related to the individual) and extrinsic factors (related to the experiment). The reliability of CPET can be investigated in relative terms, through measures such as the intraclass correlation coefficient (ICC), and in absolute terms, via the calculation of the standard error of measurement (SEM) and minimal detectable change (MDC) [3]. While both forms of reliability provide valuable insights for interpreting CPET results, they each offer distinctly different information. For example, relative reliability, in the form of ICC, indicates how likely a participant is to maintain their rank in a dataset across repeated tests. Values derived from ICC represent the proportion of variance in the measure that is attributed to true differences, with 0 indicating that all variance is due to error and 1 indicating that any difference is attributable to true differences between individuals. In contrast, values derived from SEM and MDC are expressed in the units of measurement and represent the absolute difference in individual scores. Consequently, established SEM and MDC values can be used to determine if observed changes are representative of a change in performance or merely due to natural variation in results.

Previous research indicates that commonly cited gas exchange variables such as $\dot{V}O_2$ and $\dot{V}CO_2$ exhibit excellent relative reliability across a spectrum of clinical cohorts, ranging from heart failure and valvular heart disease to pulmonary arterial hypertension [4—9]. A variable less commonly derived from CPET is the oxygen pulse ($\dot{O}_2Pulse$), which is defined as the volume of oxygen utilised per heartbeat ($\dot{V}O_2/heart\ rate$ [HR]) and is commonly expressed in mL·beat^{-1} [10]. $\dot{O}_2Pulse$ allows for the estimation of stroke volume (SV) during CPET through a simple modification of the Fick equation, in which $\dot{V}O_2$ is equal to the product of cardiac output ($\dot{Q}$) multiplied by the arteriovenous oxygen difference ($_{a-v}\dot{O}_{2diff}$).

$\dot{O}_2$*Pulse*, its derivatives, and the morphology of its associated curve when plotted against work rate, have emerged as valuable but contentious tools in the assessment of patients with suspected or documented coronary artery disease (CAD) [11—22]. The shape of the $\dot{O}_2$*Pulse* curve provides important information about the health of the cardiovascular system and its ability to deliver oxygen to working muscles. The normal trajectory of this slope in healthy individuals is suggested to be a linear increase in *y* ($\dot{O}_2$*Pulse*) in response to *x* (work-rate), reflecting an incremental rise in $\dot{Q}$ resulting from commensurate increases in both HR and SV [23]. However, an early plateau or inflection in the slope of $\dot{O}_2$*Pulse* (in those who do not reach ≥ 90% predicted $\dot{V}O_2$) is suggested to be evidence of a sudden reduction in the normal progression of SV [14,15,19]. Reductions in SV during CPET are hypothesised to occur secondary to wall motion abnormalities caused by myocardial ischaemia [13].

Previous studies have established the reliability of peak $\dot{O}_2$*Pulse* ($\dot{O}_2P_{peak}$) and or $\dot{O}_2$*Pulse* at first ventilatory threshold ($VT_1\dot{O}_2P$) [4,8,24,25]. In 1996, Lehman and Kölling found correlation coefficients for $\dot{O}_2P_{peak}$ and $VT_1\dot{O}_2P$ were $r = 0.980$; $P > 0.001$ and $r = 0.991$; $P > 0.0001$ respectively [8]. Similarly, $\dot{O}_2P_{peak}$ reliability was reported by Barron et al. in 2014 (CV of 8% and an ICC of 0.96 [95% CI = 0.94—0.97]) after recruiting 93 patients with either valvular heart disease ($n = 26$), heart failure ($n = 43$) or COPD ($n = 24$).

Although $\dot{O}_2P_{peak}$ is a valid, and potentially clinically important variable of interest, quantifying its relative reliability alone does not provide a complete assessment of all the characteristics of the $\dot{O}_2$*Pulse* curve, including the inflection points. The peak in $\dot{O}_2$*Pulse* along with its relative and absolute reliability provide information solely on its magnitude (*y* axis) telling nothing of its relation to work rate or indeed time (*x* axis). The slope of $\dot{O}_2$*Pulse* can illustrate the rate of increase in magnitude (*y* axis) over work rate or time (*x* axis) but is impacted if data is not linear, which is often the case with $\dot{O}_2$*Pulse*, at least at the later stages of exercise. The area under the curve is a variable often used in nutrition and biochemistry to demonstrate the total magnitude of response in *y* over *x*, and thus is calculated here in alongside $\dot{O}_2$*Pulse* peak and slope. Taken in combination the relative and absolute reliability of these three variables may provide more insight into $\dot{O}_2$*Pulse* morphology as a whole.

To date only two studies have attempted to investigate the stability of the curve, either in its entirety or at multiple intersects [24,25]. Moreover, both studies utilised extended test-retest intervals to establish the long-term stability of the $\dot{O}_2$*Pulse* curve. To the best of our knowledge no study to date has sought to establish the short-term relative and absolute reliability of multiple $\dot{O}_2$*Pulse* curve parameters. Determining the within-subject variability of a wider range of $\dot{O}_2$*Pulse* components, such as its slope and area under the curve, may provide a greater understanding of $\dot{O}_2$*Pulse* morphology and its underlying reliability, which may have important implications for exercise prescription, risk stratification, and rehabilitation in a variety of clinical populations. Therefore, the aim of this research was to retrospectively examine repeated CPETs with a short test-retest interval (≤ 72 hours) to determine the relative (ICC), and absolute reliability (SEM and MDC) of multiple components of the $\dot{O}_2$*Pulse* curve in healthy recreationally active participants.

2. Materials and methods

This was a single site, retrospective reliability study. Twelve, apparently healthy, recreationally active male participants were recruited between March 2017 and June 2017. Prior to testing all participants completed a pre-exercise medical questionnaire and provided written informed consent. The study was granted institutional ethical approval from the University of Hull's Sport, Health and Exercise Science Ethics Committee (AN — 8765012) on the 25 January 2017, and conducted in accordance with the Declaration of Helsinki [26]. The anonymised data for this retrospective analysis was accessed from 26 September 2022.

2.1. Study design

As this is a retrospective analysis, no a priori calculations were performed. The sample size for the original study was based on convenience, with participants recruited according to their availability and willingness during the original data collection period. Participants attended the laboratory on two occasions, the first of which included anthropometric data collection and a CPET taken to volitional exhaustion on a cycle ergometer. The second visit commenced ≤ 72 hours post, to ensure an adequate period of recovery between visits was observed. During the second visit the CPET was repeated under the same experimental conditions and with the same test equipment and administrator as visit one. The cycle ergometer (Lode Excalibur, Groningen, Netherlands) and metabolic cart (Jaegger OxyCon Pro, Hoechberg, Germany) were serviced and calibrated in line with manufacturers recommendations and guidelines prior to testing. Both tests were scheduled at the same time of day to account for diurnal variations.

2.2. Cardiopulmonary exercise tests

Each participants CPET followed a standardised incremental ramp protocol, consisting of a 5-minute rest phase, 5-minute warm-up phase (50 watts), continuous test phase (50 watts; increasing by 20 watts per minute), and finishing with a 5-minute recovery phase. The test administrator instructed each participant to maintain a cadence of ≥ 60 revolutions per minute (RPM) for the duration of each test. Participants were asked to provide their rating of perceived exertion (RPE) every two minutes during the ramp phase of the test. Tests were considered to be maximal if there was an identifiable plateau in $\dot{V}O_2$, or if $\dot{V}O_2$ failed to increase by more than 150 $mL \cdot min^{-1}$ despite increasing workload. In the absence of these findings, tests were still considered maximal providing ≥ 2 of the following was achieved [27]:

- HR failed to increase despite increasing work;
- respiratory exchange ratio (RER) ≥ 1.10;
- RPE at peak exercise ≥ 7.

2.3. Data processing

Breath-by-breath data were filtered prior to export into Microsoft Excel using a 30 second time average. This time average data was then further filtered to remove potential outlying values using a centred 9-point moving average. Whilst this layered filtering is not a common practice in the field of exercise physiology it has been used previously to reduce noise in CPET data [28], a representative example of how this impacts the data is presented in Fig. 1. Both CPETs were assessed to determine the lowest peak workload (watts), each test was then analysed at 50, 60, 70, 80, 90, and 100% of this value. Variables calculated from the data were the area under the curve (AUC) and the slope of $\dot{O}_2Pulse$ in relation to work-rate ($\dot{O}_2Pulse/\Delta WR$). Data processing was undertaken in RStudio using the R programming language. The AUC was derived from the trapezoidal method whilst the slope was calculated as the linear regression of $\dot{O}_2Pulse$ on work-rate.

2.4. Statistical analysis

Statistical analysis was performed in RStudio version 4.2.2 (Integrated Development for R. PBC, Boston, MA, USA). Descriptive statistics are presented as mean $\pm$ standard deviation (SD) unless otherwise stated. Assumptions of normality and homogeneity were tested through Shapiro-Wilk and Levene's test respectively. Test-retest reliability was determined via a two-way random effects model ICC (2,1) for absolute agreement as recommended by Koo and Li [29] and expressed with 95% confidence intervals (CI). Absolute agreement was expressed as SEM.

$$SEM = \frac{SD_{diff}}{\sqrt{2}}$$

Where SD_{diff} is the standard deviation of the difference between visits, and MDC.

$$MDC = 1.96 \times SEM \times \sqrt{2}$$

Each measure has the advantage of being expressed in its original unit of measure (e.g., mL·beat^{-1}) but was also expressed here as a percentage of the grand mean (sample mean). This dual expression is particularly beneficial because it allows for a more nuanced understanding of the data. For instance, in samples with lower (clinical) or higher mean values (athletic), the relative magnitude of the values would be impacted. Displaying these measures as percentages of the grand mean allows for more accurate comparisons of the measurement error across different cohorts. This approach facilitates the interpretation of data by normalising the error relative to the typical values observed in each sample, thus enhancing the robustness and generalisability of the findings.

3. Results

Eleven of the twelve males recruited to the study completed both CPETs within the designated window (27 $\pm$ 6 years, $\dot{V}O_{2\,max}$, 41.8 $\pm$ 9.8 mL·kg·min^{-1}). One participant was removed from the analysis due to an equipment malfunction. The remaining cohort (n = 11) completed testing without any adverse events. Maximal test criteria were achieved by ten participants for both CPETs. There was a 1.5 mL·kg·min^{-1} increase in $\dot{V}O_2$ (P = 0.032, 41.8 $\pm$ 9.8–43.3 $\pm$ 8.5 mL·kg·min^{-1}) and a 18.6 W increase in peak power (P = 0.015, 236 $\pm$ 23.9–255 $\pm$ 28.7 W) between visits one and two.

Results of the reliability and agreement analysis are presented in Table 1. The ICC values for filtered and unfiltered $\dot{O}_2P_{peak}$ and AUC across all percentages of peak work rate were statistically significant ($P \leq 0.05$). The 95% CI for $\dot{O}_2Pulse$ and $\dot{O}_2Pulse$ slope are inconsistent, ranging from poor to excellent. However, the 95% CI for $\dot{O}_2Pulse$ AUC values, both filtered and unfiltered never dropped below 0.96, indicating consistently excellent reliability. The mean difference in $\dot{O}_2P_{peak}$ between visits was 0.19 $\pm$ 0.94 and 0.21 $\pm$ 0.82 mL·beat^{-1} for unfiltered and filtered data respectively. The SEM and MDC expressed as a percentage of the grand mean for all three variables are presented in Fig. 2. Clearly, error as a percentage is more consistent in the filtered version of the data. It also appears that the $\dot{O}_2Pulse$ slope has a greater degree of error when taken at the middle rather than the end of the test, which is perhaps to be expected, as the former presents less data points with which to formulate a precise slope than the latter.

4. Discussion

The aim of the study was to determine the reliability and agreement of multiple parameters of the $\dot{O}_2Pulse$ curve for CPETs undertaken $\leq$ 72 hours apart. The data indicates that $\dot{O}_2Pulse$, its slope and the AUC taken at 50–100% of peak workload are reliable in both their filtered and unfiltered forms. However, the most optimal parameter for reliability is the filtered $\dot{O}_2Pulse$ AUC. For all percentage ranges tested, the filtered $\dot{O}_2Pulse$ AUC returned statistically significant ($P \leq 0.05$) ICC values, which in accordance with the literature can be classified as excellent (95% CI = $\geq$ 0.95–1.00) [29].

The mean %MDC for filtered AUC was 15 $\pm$ 0.8 ranging from 14.1 at 100 to 13.5 at 50% peak work-rate. In contrast, the mean %MDC for filtered $\dot{O}_2Pulse$ and $\dot{O}_2Pulse$ slope were 13.5 $\pm$ 3.2 and 121.1 $\pm$ 90.9 respectively. It is perhaps not surprising that the error is greatest for the slope, especially at the lower percentages of work, whereby virtue of the test length there are less data points with which to formulate a replicable slope. The fact that the %MDC for both $\dot{O}_2Pulse$ and $\dot{O}_2Pulse$ AUC are so similar and consistent across percentages of work is not at all surprising, as the former is used to calculate the latter. The similarity between the percentage error in $\dot{O}_2Pulse$ and $\dot{O}_2Pulse$ AUC implies that the morphology of the slope itself is replicable.

The results of the present study are in accordance with previous findings, suggesting various parameters measured with metabolic gas carts during CPETs produce excellent reliability (ICC = $\geq$ 0.9) [4–9]. Barron et al. [4] reported an ICC value of 0.96 (95% CI = 0.94 - 0.97) for $\dot{O}_2P_{peak}$ with a CV of 8%. The authors recruited 93 patients with either valvular heart disease (n = 26), heart failure (n = 43) or COPD

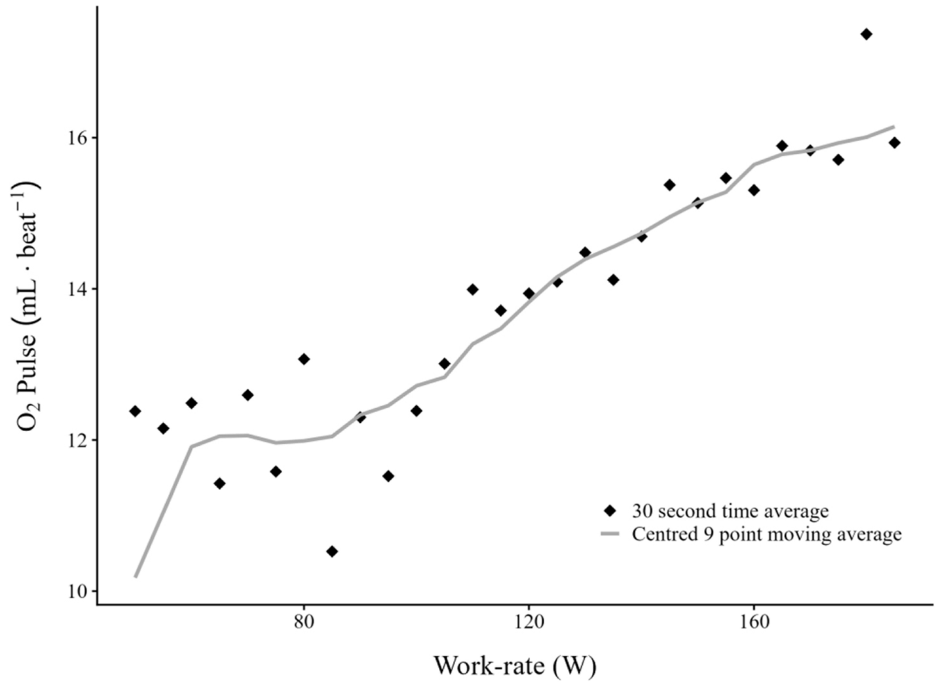

Figure 1 Representative example of layered filtering's impact upon the 30s averaged data.

($n = 24$). In this instance, repeated CPET were performed on a cycle ergometer but were not identical. For the first test each patient generically undertook a 10 watt per minute ramp protocol, with the second test tailored to the individual based upon the results of the first [4]. The authors concede that this is not ideal for reproducibility, however they contend it is more likely to occur in clinical settings. Whilst true this does impact the generalisability of the results and comparisons to our findings, as conditions, namely the work rate slope, were not held constant between visits.

As mentioned in the introduction, the relative and absolute reliability of additional components of the $\dot{O}_2Pulse$ slope, relating more to its morphology, may be of greater clinical significance. To this end Perim and colleagues recruited $n = 49$ professional footballers (18—31 years) from the 1st divisions of Brazil and Angola and conducted repeated CPETs [25]. Each CPET was treadmill-based, utilising a ramp protocol. The tests themselves were separated by a mean of 12 months (range 2—24). $\dot{O}_2Pulse$ was compared every 10% of effective running time (≥ 8 km/h) for both tests and expressed normalised to body mass (mL·beat·kg^{-1}). The authors used coefficients of determination (R^2) at each percentage point as a measure of reliability. They concluded that mean values of the coefficients were ''virtually identical'' for the first and second tests at 0.64 and 0.63 respectively [25]. Clearly these values are exceptionally close to one another, but they only indicate that between 63 and 64% of the variation in the $\dot{O}_2Pulse$ curve during CPET can be explained by the treadmill velocity. Perhaps a more informative parameter for the reliability of the $\dot{O}_2Pulse$ curve explored by the authors was the slope and intercept. The study indicated no statistically significant differences between the slopes ($P = 0.44$) or intersects ($P = 1.00$), indicating that $\dot{O}_2Pulse$ at onset and increase throughout the CPET was indeed repeatable even when separated by 2—24 months. This paper is limited by the large variability in test-retest interval, and by the fact that the second CPET was taken to volitional exhaustion. As a result, participants achieved a significantly greater maximal velocity ($P < 0.01$) and exercise duration. This would have generated a rightward shift in the scale of effective running time and resulted in the comparison of $\dot{O}_2Pulse$ values elicited by different work-rates (WR). Furthermore, the authors used coefficients of determination and significance testing instead of absolute agreement metrics, such as SEM or MDC, which would have provided a quantitative parameter beyond which true change could be accepted.

The long-term stability of the $\dot{O}_2Pulse$ curve was also investigated by Olivera and colleagues in 2011. In this instance the authors retrospectively examined the $\dot{O}_2Pulse$ curve in 100 pairs of CPETs (80 male) [24]. Participants (mean 59 years $\pm$ 12 years) were non-athletes for whom repeated test data was available with a minimum 3 month separation (median 15 months; range 5—62). Tests were completed either for clinical or exercise prescription purposes. Both tests were performed on an electronically braked cycle ergometer using a personalised ramp protocol. The authors found that $\dot{V}O_{2peak}$ (11%) and $\dot{O}_2P_{peak}$ (10%) were significantly increased during the second CPET ($P = 0.004$ and $P = 0.002$), respectively. However, when separated into quintiles based upon $\dot{O}_2P_{peak}$ normalised to body mass, values achieved in the second CPET were not statistically significantly different in either their slope or intercept from the initial test, with the exception of the intercept in quintile 5 ($P = 0.007$). These findings were maintained in a subset analysis of slopes in patients with known CAD ($P = 0.031$). As with the findings of Perim and colleagues [25] there was no effort made to establish absolute agreement through SEM or MDC, which limits the utility of the results. Furthermore, 75% of the

Table 1 Reliability and agreement tests at each percentage of peak work-rate.

Variable	% of peak work-rate	Mean ± SD	ICC	95% CI	*P*-value	*F*	SEM	MDC
$\dot{O}_2Pulse$ (mL·beat^{-1})	50	14,259 ± 3129	0.95	0.84–0.99	$P < 0.001$	22	0.984	2.726
	60	14,886 ± 3386	0.95	0.81–0.99	$P < 0.001$	18	1.139	3.158
	70	16,000 ± 3475	0.95	0.82–0.99	$P < 0.001$	20	1.096	3.039
	80	16,968 ± 3507	0.97	0.89–0.99	$P < 0.001$	33	0.907	2.515
	90	18,045 ± 3839	0.98	0.92–0.99	$P < 0.001$	45	0.859	2.381
	100	19,032 ± 4044	0.99	0.96–1.00	$P < 0.001$	81	0.662	1.835
Filtered $\dot{O}_2Pulse$ (mL·beat^{-1})	50	14,200 ± 3955	0.97	0.89–0.99	$P < 0.001$	31	0.650	2.166
	60	15,036 ± 3283	0.96	0.87–0.99	$P < 0.001$	27	0.657	2.575
	70	15,995 ± 3324	0.96	0.88–0.99	$P < 0.001$	28	0.595	2.510
	80	16,986 ± 3526	0.98	0.92–0.99	$P < 0.001$	43	0.589	2.203
	90	18,027 ± 3722	0.98	0.94–1.00	$P < 0.001$	60	0.652	1.990
	100	18,641 ± 3955	0.99	0.96–1.00	$P < 0.001$	98	0.539	1.615
$\Delta\dot{O}_2Pulse/\Delta$WR slope (mL·beat·W)	50	0.020 ± 0.060	0.93	0.77–0.98	$P < 0.001$	15	0.022	0.062
	60	0.024 ± 0.030	0.72	−0.00–0.92	$P = 0.030$	3.5	0.021	0.059
	70	0.034 ± 0.020	0.67	−0.18–0.91	$P = 0.049$	3	0.015	0.041
	80	0.039 ± 0.017	0.73	0.04–0.93	$P = 0.025$	3.7	0.012	0.033
	90	0.042 ± 0.015	0.74	0.75–0.93	$P = 0.023$	3.8	0.010	0.028
	100	0.044 ± 0.014	0.84	0.42–0.96	$P = 0.004$	6.1	0.008	0.022
Filtered $\Delta\dot{O}_2Pulse/\Delta$WR slope (mL·beat·W)	50	0.018 ± 0.022	0.49	−0.83–0.86	$P = 0.153$	2	0.019	0.054
	60	0.028 ± 0.019	0.56	−0.55–0.88	$P = 0.026$	2.3	0.016	0.043
	70	0.034 ± 0.017	0.60	−0.41–0.89	$P = 0.080$	2.5	0.013	0.037
	80	0.039 ± 0.015	0.72	0.00–0.92	$P = 0.029$	3.6	0.011	0.029
	90	0.042 ± 0.014	0.79	0.26–0.94	$P = 0.011$	4.7	0.009	0.024
	100	0.042 ± 0.014	0.87	0.54–0.96	$P = 0.002$	7.7	0.007	0.019
$\dot{O}_2Pulse$ AUC (mL·W·beat^{-1})	50	316.280 ± 173,270	1.00	0.98–1.00	$P < 0.001$	221	17.603	48.792
	60	609.885 ± 274,781	0.99	0.97–1.00	$P < 0.001$	129	36.543	101.292
	70	919.700 ± 341,800	0.99	0.96–1.00	$P < 0.001$	91	53.890	149.375
	80	1261.073 ± 469,718	0.99	0.96–1.00	$P < 0.001$	91	73.582	203.959
	90	1623.182 ± 568,588	0.99	0.96–1.00	$P < 0.001$	92	88.944	246.540
	100	2005.305 ± 696,886	0.99	0.97–1.00	$P < 0.001$	109	99.865	276.812
Filtered $\dot{O}_2Pulse$ AUC (mL·W·beat^{-1})	50	319.046 ± 176,296	1.00	0.99–1.00	$P < 0.001$	272	16.218	44.953
	60	612.997 ± 275,219	0.99	0.98–1.00	$P < 0.001$	149	34.064	94.420
	70	924.286 ± 342,603	0.99	0.96–1.00	$P < 0.001$	100	51.568	142.927
	80	1265.018 ± 469,447	0.99	0.96–1.00	$P < 0.001$	99	70.760	196.136
	90	1628.368 ± 568,862	0.99	0.96–1.00	$P < 0.001$	98	85.951	238.243
	100	2005.691 ± 697,074	0.99	0.97–1.00	$P < 0.001$	114	97.568	270.445

SD: standard deviation; ICC: intraclass correlation coefficient; CI: confidence interval; SEM: standard error of measure; MDC: minimal detectable change.

study cohort participated in a supervised exercise intervention three times per week, whilst the remaining 25% were supplied with exercise related advice [24], both of these interventions could have impacted upon the stability of the $\dot{O}_2Pulse$ curve.

Clearly caution should be taken when comparing these results with the present study, as we performed repeat tests over a period of days and compared only the responses to percentages of a fixed workload. However, these findings in combination do add to the existing literature around the reliability of $\dot{O}_2Pulse$ [24,25], suggesting it is a robust and stable variable, both in the longer and shorter term.

Establishing the reliability of measures during CPET is essential. Without knowledge and confidence in the degree of error it is impossible to individualise threshold-based exercise prescriptions or accurately establish improvement following intervention. Despite the clear requirement for studies of this nature there is no consensus reporting criteria. There are many statistical methods available to quantify test-retest reliability and agreement. However, when calculated as:

$$\Rightarrow \%MDC = \frac{1.96 \times SEM \times \sqrt{2}}{Grand\ Mean} \times 100$$

The %MDC provides a boundary outside of which we can be confident true change will have occurred approximately 95% of the time. Furthermore, as this is expressed as a percentage of the sample mean (grand mean) it is consistent even with an increase in the unit measured and can be compared across studies and variables. It is our hope that presenting the results in this fashion allows them to be adopted or used for direct comparison in future research.

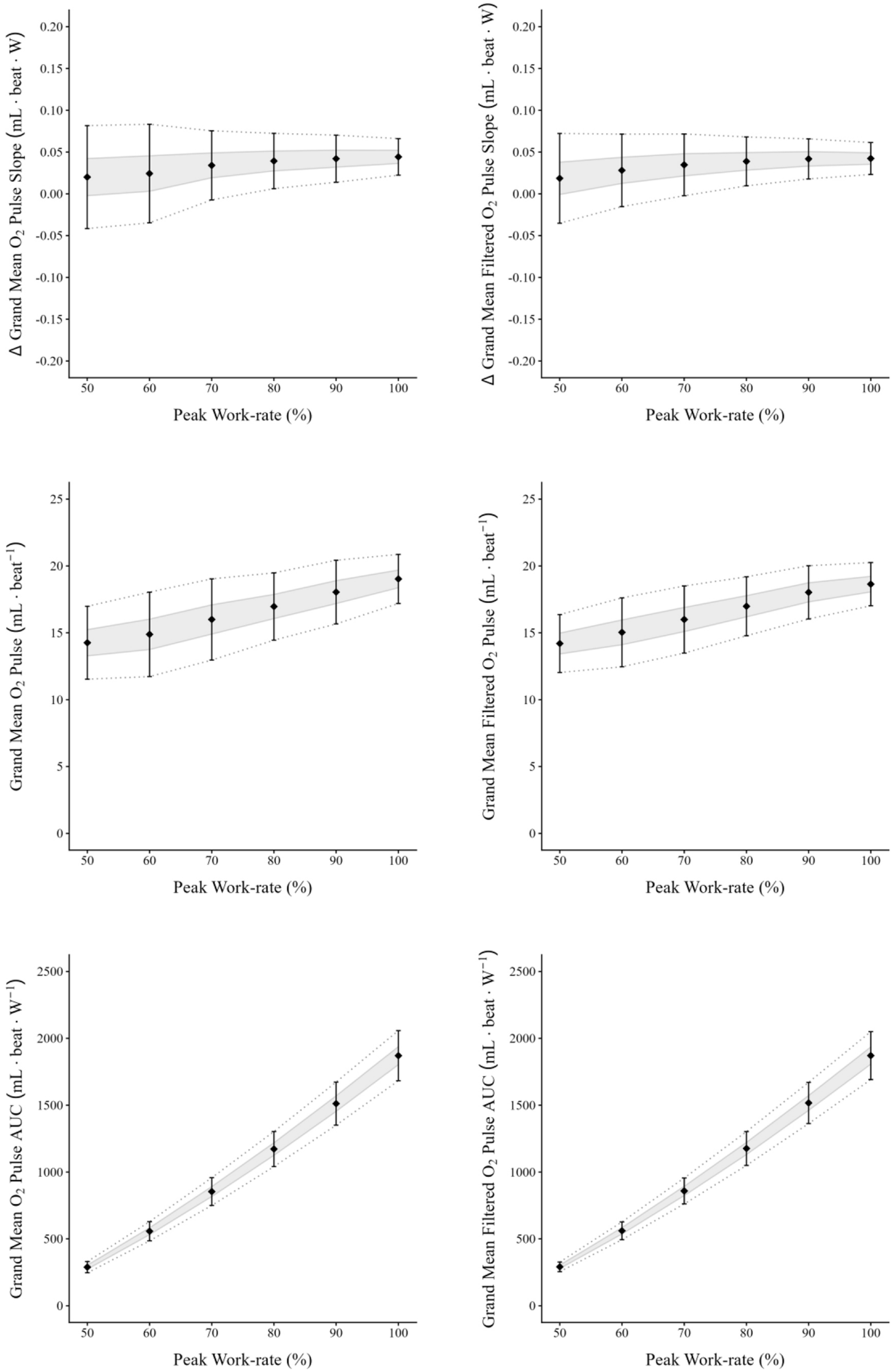

Figure 2 The SEM and MDC expressed as a percentage of the grand mean (grey = %SEM; error bars and dotted line = %MDC).

Establishing the reliability of $\dot{O}_2Pulse$ curve parameters may be of particular importance to clinicians and clinical exercise physiologists. Previous research has established that $\dot{O}_2P_{peak}$ is a significant ($P \leq 0.05$) predictor of cardiovascular and all-cause mortality in people with and without cardiovascular disease [30,31]. Furthermore, when normalised to body mass $\dot{O}_2P_{peak}$ exhibits an inverse linear relationship with cardiovascular and all-cause mortality in middle-aged men [32]. A clear understanding of $\dot{O}_2P_{peak}$ reliability is essential if it is to be used in the early identification and modification of those at increased risk, here we provide evidence that the %SEM associated with $\dot{O}_2P_{peak}$ ($\dot{O}_2Pulse$ at 100%) is 3.48 with %MDC of 9.64.

Inflections or premature plateaus in the otherwise linear increase of $\dot{O}_2Pulse$ have been linked to the onset of myocardial ischaemia [11,14,15,19]. One of the stated aims of exercise-based cardiac rehabilitation according to the Association of Chartered Physiotherapists in Cardiac Rehabilitation (ACPICR) standards [33] is to increase the ischaemic threshold. Additionally, existing training guidelines presented by the American College of Sports Medicine (ACSM) recommend outpatient-training intensities for CR to be below the ischaemic threshold (< 10 beats), or below a threshold that elicits the onset of angina symptoms [34]. If practitioners are to accurately detect the ischaemic threshold, prescribe exercise training intensity based on the threshold, and then monitor changes in the threshold following a period of exercise training, it is first necessary to determine the SEM, and more importantly MDC at multiple points across the curve. This study demonstrates that in healthy male participants the mean %MDC of $\dot{O}_2Pulse$ from 50—100% of peak work-rate is 16 ± 4.34. This does not mean that once detected the ischaemic threshold holds the same level of consistency, it does however provide a boundary outside of which increases or decreases can confidently be determined.

4.1. Limitations

This study is not without its limitations, firstly, the small sample size is more prone to the influence of outliers, which could positively or negatively skew the differences between tests. The SD of the differences is used in the calculation of SEM and MDC and thus could have artificially exaggerated the error in the sample versus the true error in the population. Secondly, the homogeneous nature of the sample, both in term of sex and age may further impact the transferability of these results. Finally, only two measures were taken for each participant, this introduces the possibility that the error observed may represent a learned effect resulting from familiarisation with the test procedure. Future research should perform a minimum of three tests, thus allowing for multiple pairwise comparisons to be made. It would then be possible to determine whether there exists a significant difference between minimal detectable changes, and ultimately whether a familiarisation visit is necessary.

5. Conclusion

This study demonstrates that when conducting a CPET, for points ranging from 50—100% of peak work-rate, the $\dot{O}_2Pulse$ has moderate to excellent reliability. Furthermore, when viewed with the AUC parameter, reliability increases to excellent (ICC $\geq$ 0.9). Previous guidelines indicate that the $\dot{O}_2Pulse$ curve should be assessed in clinical settings for the identification and assessment of CAD. Our findings not only indicate that the $\dot{O}_2Pulse$ is reliable, but will also quantify the minimal value required to be confident of true change.

Disclosure of interest

The authors declare that they have no competing interest.

Références

[1] Taylor C, Nichols S, Ingle L. A clinician's guide to cardiopulmonary exercise testing 1: an introduction. Br J Hosp Med (Lond) 2015;76:192—5, http://dx.doi.org/10.12968/hmed.2015.76.4.192.

[2] Otto JM, Levett DZH, Grocott MPW. Cardiopulmonary exercise testing for preoperative evaluation: what does the future hold? Curr Anesthesiol Rep 2020;10:1—11, http://dx.doi.org/10.1007/s40140-020-00373-x.

[3] Wilkinson TJ, Xenophontos S, Gould DW, et al. Test-retest reliability, validation, and ''minimal detectable change'' scores for frequently reported tests of objective physical function in patients with non-dialysis chronic kidney disease. Physiother Theory Pract 2019;35:565—76, http://dx.doi.org/10.1080/09593985.2018.1455249.

[4] Barron AJ, Dhutia NM, Mayet J, et al. Test-retest repeatability of cardiopulmonary exercise test variables in patients with cardiac or respiratory disease. Eur J Prev Cardiol 2014;21:445—53, http://dx.doi.org/10.1177/2047487313518474.

[5] Bensimhon D, Leifer ES, Ellis SJ, et al. Reproducibility of peak oxygen uptake and other cardiopulmonary exercise testing parameters in patients with heart failure (from the Heart Failure and A Controlled Trial Investigating Outcomes of exercise traiNing). Am J Cardiol 2008;102:712—7, http://dx.doi.org/10.1016/j.amjcard.2008.04.047.

[6] Hansen JE, Sun XG, Yasunobu Y, et al. Reproducibility of cardiopulmonary exercise measurements in patients with pulmonary arterial hypertension. Chest 2004;126:816—24, http://dx.doi.org/10.1378/chest.126.3.816.

[7] Marburger C, Brubaker P, Pollock W, et al. Reproducibility of cardiopulmonary exercise testing in elderly patients with congestive heart failure. Am J Cardiol 1998;82:905—9, http://dx.doi.org/10.1016/s0002-9149(98)00502-5.

[8] Lehmann G, Kölling K. Reproducibility of cardiopulmonary exercise parameters in patients with valvular heart disease. Chest 1996;110:685—92, http://dx.doi.org/10.1378/chest.110.3.685.

[9] Skinner JS, Wilmore KM, Kristine M, et al. Reproducibility of maximal exercise test data in the HERITAGE family study. Med Sci Sports Exerc 1999;31:1623—8, http://dx.doi.org/10.1097/00005768-199911000-00020.

[10] Nichols S, Taylor C, Ingle L. A clinician's guide to cardiopulmonary exercise testing 2: test interpretation. Br J Hosp Med (Lond) 2015;76:281—9, http://dx.doi.org/10.12968/hmed.2015.76.5.281.

[11] Huang S, Wang L, Li J, et al. Oxygen pulse variation in symptomatic patients with suspected coronary artery disease: a diagnostic analysis. Ann Transl Med 2022;10(22):1—10, http://dx.doi.org/10.21037/atm-22-5279.

[12] De Lorenzo A, Da Silva CL, Da Silva CL, et al. Value of the oxygen pulse curve for the diagnosis of coro-

nary artery disease. Physiol Res 2018;67:679—86, http://dx.doi.org/10.33549/physiolres.933788.
[13] De Lorenzo A, da Silva CL, Souza FCC, et al. Clinical, scintigraphic, and angiographic predictors of oxygen pulse abnormality in patients undergoing cardiopulmonary exercise testing. Clin Cardiol 2017;40:914—8, http://dx.doi.org/10.1002/clc.22747.
[14] Belardinelli R, Lacalaprice F, Carle F, et al. Exercise-induced myocardial ischaemia detected by cardiopulmonary exercise testing. Eur Heart J 2003;24:1304—13, http://dx.doi.org/10.1016/s0195-668x(03)00210-0.
[15] Belardinelli R, Lacalaprice F, Tiano L, et al. Cardiopulmonary exercise testing is more accurate than ECG-stress testing in diagnosing myocardial ischemia in subjects with chest pain. Int J Cardiol 2014;174:337—42, http://dx.doi.org/10.1016/j.ijcard.2014.04.102.
[16] Chaudhry S, Arena R, Hansen JE, et al. The utility of cardiopulmonary exercise testing to detect and track early-stage ischemic heart disease. Mayo Clin Proc 2010;85:928—32, http://dx.doi.org/10.4065/mcp.2010.0183.
[17] Chaudhry S, Arena R, Wasserman K, et al. The utility of cardiopulmonary exercise testing in the assessment of suspected microvascular ischemia. Int J Cardiol 2011;148:7—9, http://dx.doi.org/10.1016/j.ijcard.2009.01.055.
[18] Peterman JE, Harber MP, Chaudhry S, et al. Peak oxygen pulse and mortality risk in healthy women and men: the Ball State Adult Fitness Longitudinal Lifestyle Study (BALL ST). Prog Cardiovasc Dis 2021;1(68):19—24, http://dx.doi.org/10.1016/j.pcad.2021.07.001.
[19] Chaudhry S, Arena R, Wasserman K, et al. Exercise-induced myocardial ischemia detected by cardiopulmonary exercise testing. Am J Cardiol 2009;103:615—9, http://dx.doi.org/10.1016/j.amjcard.2008.10.034.
[20] de Almeida VVS, Almeida V, de Almeida FM, et al. Flattening of pulse oxygen during cardiopulmonary exercise testing (CPET) and associated factors in non-cardiopathic adults: cross-sectional results from the EPIMOV study. Eur Respir J 2018;52(62):24—74, http://dx.doi.org/10.1183/13993003.congress-2018.pa2474.
[21] Chuang M-L, Lin I-F, Huang SF, et al. Patterns of oxygen pulse curve in response to incremental exercise in patients with chronic obstructive pulmonary disease — an observational study. Sci Rep 2017;7:10929, http://dx.doi.org/10.1038/s41598-017-11189-x.
[22] Munhoz EC, Hollanda R, Vargas JP, et al. Flattening of oxygen pulse during exercise may detect extensive myocardial ischemia. Med Sci Sports Exerc 2007;39:1221—6, http://dx.doi.org/10.1249/mss.0b013e3180601136.
[23] Sietsema KE, Stringer WW, Sue DY, Ward S. In: Wasserman & Whipp's: principles of exercise testing and interpretation: including pathophysiology and clinical applications. 7th ed Philadelphia: Lippincott Williams & Wilkins; 2020.
[24] de Oliveira RB, Oliveira RB, Myers J, de Araújo CGS. Long-term stability of the oxygen pulse curve during maximal exercise. Clinics 2011;66:203—9, http://dx.doi.org/10.1590/s1807-59322011000200004.
[25] Perim RR, Perim RR, Signorelli GR, et al. Stability of relative oxygen pulse curve during repeated maximal cardiopulmonary testing in professional soccer players. Braz J Med Biol Res 2011;44:700—6, http://dx.doi.org/10.1590/s0100-879x2011007500073.
[26] World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA 2013;310:2191—4, http://dx.doi.org/10.1001/jama.2013.281053.
[27] American College of Sports Medicine (ACSM). ACSM's guidelines for exercise testing and prescription. 11th ed. Philadelphia: Wolters Kluwer; 2022.
[28] Nickolay T, McGregor G, Powell R, et al. Inter- and intra-observer reliability and agreement of O2Pulse inflection during cardiopulmonary exercise testing: a comparison of subjective and novel objective methodology. PLoS One 2024;19:e0299486, http://dx.doi.org/10.1371/journal.pone.0299486.
[29] Koo TK, Li MY. A guideline of selecting and reporting intraclass correlation coefficients for reliability research. J Chiropr Med 2016;15:155—63, http://dx.doi.org/10.1016/j.jcm.2016.02.012.
[30] Oliveira RB, Myers J, Araújo CGS, et al. Maximal exercise oxygen pulse as a predictor of mortality among male veterans referred for exercise testing. Eur J Cardiovasc Prev Rehabil 2009;16:358—64, http://dx.doi.org/10.1097/HJR.0b013e3283292fe8.
[31] Oliveira RB, Myers J, Araújo CGS, et al. Does peak oxygen pulse complement peak oxygen uptake in risk stratifying patients with heart failure? Am J Cardiol 2009;104:554—8, http://dx.doi.org/10.1016/j.amjcard.2009.04.022.
[32] Laukkanen JA, Kurl S, Salonen JT, et al. Peak oxygen pulse during exercise as a predictor for coronary heart disease and all cause death. Heart 2006;92:1219—24, http://dx.doi.org/10.1136/hrt.2005.077487.
[33] ACPICR. Standards for physical activity and exercise in the cardiac population. 3rd ed; 2015.
[34] American College of Sports Medicine (ACSM). ACSM's guidelines for exercise testing and prescription. Philadelphia: Wolters Kluwer; 2018.